Zhou 09/909,038

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=> d his 1

     (FILE 'MEDLINE, HCAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     13:36:27 ON 24 SEP 2003)
L22          56 DUP REM L21 (37 DUPLICATES REMOVED)

=> d que l22
L1         6564 SEA WOLF D?/AU
L2           35 SEA GERLACH O?/AU
L3          499 SEA BAERNS M?/AU
L4         7040 SEA (L1 OR L2 OR L3)
L5           19 SEA L4 AND CATALY? AND EVOLUTION?
L6           11 SEA L5 AND COMBINATORIAL?
L8          356 SEA CATALY? AND EVOLUTION? AND COMBINATORIAL?
L9           61 SEA RANDOM AND L8
L10          18 SEA STOCHAS? AND L8
L11          78 SEA (L9 OR L10) AND (RECOMBIN? OR CROSS? OR MUTAT? OR STRUCTUR?
                 OR COMBIN? OR COMPOS?)
L12          74 SEA L11 NOT L6
L13         102 SEA L8 AND GENERAT?
L14           1 SEA L13 AND RESTRUCTUR?
L15          75 SEA L12 OR L14
L16        1016 SEA RANDOM(5A) GENERATOR
L17           3 SEA L16 AND CATALY?
L18          78 SEA L15 OR L17
L19          34 SEA L8 AND GENERATION?
L20         100 SEA L18 OR L19
L21          93 SEA L20 NOT L6
L22          56 DUP REM L21 (37 DUPLICATES REMOVED)


=> d ibib abs l22 1-56

L22  ANSWER 1 OF 56     MEDLINE on STN                    DUPLICATE 1
ACCESSION NUMBER:    2003068512     MEDLINE
DOCUMENT NUMBER:     22466567   PubMed ID: 12578373
TITLE:               Altering substrate specificity of phosphatidylcholine-
                     preferring phospholipase C of Bacillus cereus by
                     random mutagenesis of the headgroup binding site.
AUTHOR:              Antikainen Nina M; Hergenrother Paul J; Harris Micheleen M;
                     Corbett William; Martin Stephen F
CORPORATE SOURCE:    Department of Chemistry and Biochemistry and The Institute
                     of Cellular and Molecular Biology, The University of Texas,
                     Austin, Texas 78712, USA.
CONTRACT NUMBER:     GM 42763 (NIGMS)
SOURCE:              BIOCHEMISTRY, (2003 Feb 18) 42 (6) 1603-10.
                     Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         200305
ENTRY DATE:          Entered STN: 20030212
                     Last Updated on STN: 20030503
                     Entered Medline: 20030502
AB   PLC(Bc) is a 28.5 kDa monomeric enzyme that catalyzes the
     hydrolysis of the phosphodiester bond of phosphatidylcholine,
     phosphatidylethanolamine, and phosphatidylserine to provide a
     diacylglycerol and the corresponding phosphorylated headgroup.  Because
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Search completed by David Schreiber 308-4292

single replacements of Glu4, Tyr56, and Phe66 in the headgroup binding pocket led to changes in substrate specificity [Martin et al. (2000) Biochemistry 39, 3410-3415], a **combinatorial** library of approximately 6000 maltose binding protein-PLC(Bc) fusion protein mutants containing **random** permutations of these three residues was generated to identify PLC(Bc) mutants with altered specificity profiles and high **catalytic** activities. Members of this library were screened for hydrolytic activity toward the water soluble substrates C6PC, C6PE, and C6PS using a novel protocol that was conducted in a 96-well format and featured the in situ cleavage of the fusion protein to release the mutant PLC(Bc)s. Ten mutant enzymes that exhibited significant preferences toward C6PE or C6PS were selected and analyzed by steady-state kinetics to determine their specificity constants, k(cat)/K(M). The C6PS selective clones E4G, E4Q/Y56T/F66Y, and E4K/Y56V exhibited higher specificity constants toward C6PS than wt, whereas Y56T, F66Y, and Y56T/F66Y were C6PE selective and had comparable or higher specificity constants than wt for C6PE. The corresponding wt residues were singly reinserted back into the E4Q/Y56T/F66Y and E4K/Y56V mutants via site-directed mutagenesis, and the E4Q/F66Y mutant thus obtained exhibited a 10-fold higher specificity constant toward C6PS than wt, a value significantly higher than other PLC(Bc) mutants. On the basis of available data, an aromatic residue at position 66 appears important for significant **catalytic** activity toward all three substrates, especially C6PC and C6PE. The charge of residue 4 also appears to be a determinant of enzyme specificity as a negatively charged residue at this position endows the enzyme with C6PC and C6PE preference, whereas a polar neutral or positively charged residue results in C6PS selectivity. Replacing Tyr56 with Val, Ala, Thr, or Ser greatly reduces activity toward C6PC. Thus, the substrate specificity of PLC(Bc) can be modulated by varying three of the amino acid residues that constitute the headgroup binding pocket, and it is now apparent that this enzyme is not **evolutionarily** optimized to hydrolyze phospholipids with ethanolamine or serine headgroups.

L22 ANSWER 2 OF 56 MEDLINE on STN
ACCESSION NUMBER: 2003009734 MEDLINE
DOCUMENT NUMBER: 22404052 PubMed ID: 12515480
TITLE: The combined solid/solution-phase synthesis of nitrosamines: the **evolution** of the "libraries from libraries" concept.
AUTHOR: Yu Yongping; Ostresh John M; Houghten Richard A
CORPORATE SOURCE: Torrey Pines Institute for Molecular Studies, 3550 General Atomics Court, San Diego, California 92121, USA.
CONTRACT NUMBER: CA78040 (NCI)
SOURCE: JOURNAL OF ORGANIC CHEMISTRY, (2003 Jan 10) 68 (1) 183-6. Journal code: 2985193R. ISSN: 0022-3263.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200306
ENTRY DATE: Entered STN: 20030108
Last Updated on STN: 20030621
Entered Medline: 20030620

AB The **generation** of diverse chemical libraries using the "libraries from libraries" concept by combining solid-phase and solution-phase methods is described. The central features of the approaches presented are the use of solid-phase synthesis methods for the **generation** of a **combinatorial** polyamine library.

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Following cleavage from the resin with HF, the polyamine library was reacted with ethyl nitrite in the solution phase to yield the desired nitrosamine library in good yield and purity. The approaches described enable the efficient syntheses of individual nitrosamines as well as mixture-based nitrosamine libraries.

L22 ANSWER 3 OF 56 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 2003:511941 SCISEARCH
THE GENUINE ARTICLE: 689CK
TITLE: Application of genetic algorithm to optimize the composition of Cu-Zn-Al-Sc oxide **catalyst** for methanol synthesis
AUTHOR: Umegaki T; Omata K; Ishiguro G; Watanabe Y; Yamada M (Reprint)
CORPORATE SOURCE: Tohoku Univ, Grad Sch Engn, Dept Appl Chem, Aoba Ku, Aoba 07, Sendai, Miyagi 9808579, Japan (Reprint); Tohoku Univ, Grad Sch Engn, Dept Appl Chem, Aoba Ku, Sendai, Miyagi 9808579, Japan
COUNTRY OF AUTHOR: Japan
SOURCE: JOURNAL OF THE JAPAN PETROLEUM INSTITUTE, (MAY 2003) Vol. 46, No. 3, pp. 181-188.
Publisher: JAPAN PETROLEUM INST, COSMO HIRAKAWA-CHO BLDG, 3-14, 1-CHOME HIRAKAWA-CHO, CHIYODA-KU, TOKYO, 102, JAPAN.
ISSN: 1346-8804.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 20
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB A genetic algorithm (GA), which is based on the theory of biological **evolution**, was applied to optimize the composition of Cu-Zn-Al-Sc oxide **catalyst** for methanol synthesis to identify high performance **catalysts** faster and more effectively. Using our own GA program where the activities from experiments were used as the fitness, we could almost optimize the composition by the fifth **generation** . The **catalyst** with maximum activity at the fifth **generation** had higher Cu/Zn ratio than conventional **catalysts**. The GA is a powerful tool to optimize **catalyst** composition.

L22 ANSWER 4 OF 56 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2003132837 IN-PROCESS
DOCUMENT NUMBER: 22534113 PubMed ID: 12646690
TITLE: **Evolutionary** engineering of a beta-Lactamase activity on a D-Ala D-Ala transpeptidase fold.
AUTHOR: Peimbert Mariana; Segovia Lorenzo
CORPORATE SOURCE: Departamento de Ingenieria Celular y Biocatalisis, Instituto de Biotecnologia, UNAM, Av. Universidad 2001, Col. Chamilpa, Cuernavaca, Morelos, 62250 MexicoE-mail:. lorenzo@ibt.unam.mx,peimbert@ibt.unam.mx
SOURCE: PROTEIN ENGINEERING, (2003 Jan) 16 (1) 27-35.
Journal code: 8801484. ISSN: 0269-2139.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20030321
Last Updated on STN: 20030321

AB The beta-Lactamase hydrolytic activity has arisen several times from DD-transpeptidases. We have been able to replicate the

evolutionary process of beta-Lactamase activity emergence on a PBP2X DD-transpeptidase. Some of the most interesting changes, like modifying the **catalytic** properties of an enzyme, may require several **mutations** in concert; therefore it is essential to explore efficiently sequence space by generating the right diversity. We designed a biased **combinatorial** library in which biochemical and **structural** information were incorporated by site directed mutagenesis on relevant residues and then subjected to **random** mutagenesis to allow for **mutations** in unforeseen positions. We isolated mutants from this library conferring 10-fold higher cefotaxime resistance levels than the background wild-type through **mutations** exclusively in the coding sequence. We demonstrate that only three substitutions in the DD-transpeptidase active site, two produced by the directed and one by the **random** mutagenesis, are sufficient to acquire this activity. The purified product of one mutant (MutE) had a 10(5)-fold increase in cefotaxime deacylation rate allowing it to hydrolyze beta-Lactams yet it has apparently conserved DD-peptidase activity. This work is the first to show a possible **evolutionary** intermediate between a beta-Lactamase and a DD-transpeptidase necessary for the development of antibiotic resistance.

L22 ANSWER 5 OF 56 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:736370 HCAPLUS
DOCUMENT NUMBER: 137:259520
TITLE: In vitro **random** expression array library (REAL) cloning for screening a nucleic acid library and in vitro **evolution** of biomolecules with binding, **catalytic** or regulatory activities
INVENTOR(S): Sepp, Armin; Choo, Yen
PATENT ASSIGNEE(S): Sangamo Biosciences, Inc., USA
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002074915	A2	20020926	WO 2002-US7932	20020315

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2001-6636 A 20010316

AB An in vitro method is provided for isolating from a plurality of nucleotide sequences a clone that encodes either a polypeptide or an polynucleotide mol. having desired binding, regulatory or **catalytic** activity. The method is based on in vitro transcription or translation from aliquots of pooled nucleotide sequences, identification of the pools encoding the desired activity and subdivision of the selected pools into subpools with reduced complexity until the desired activity is isolated.

Search completed by David Schreiber 308-4292

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L22 ANSWER 6 OF 56 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:69368 HCAPLUS
DOCUMENT NUMBER: 136:108039
TITLE: Evolutionary method for the preparation and selection of new **catalysts**
INVENTOR(S): Wolf, Dorit; Gerlach, Olga; Baerns, Manfred
PATENT ASSIGNEE(S): Institut fuer Angewandte Chemie Berlin-Adlershof e.V., Germany
SOURCE: Eur. Pat. Appl., 13 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1174186	A2	20020123	EP 2001-250270	20010719
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
DE 10037166	A1	20020207	DE 2000-10037166	20000720
US 2002076726	A1	20020620	US 2001-909038	20010719

PRIORITY APPLN. INFO.: DE 2000-10037166 A 20000720

AB Improved evolutionary method for the prepn. and selection of new **catalysts** is a stochastic method including crossing and mutation to determinate the new **catalyst** compn. and the performance parameters of the **catalyst** generations. The detn. of the new **catalyst** compn. results in following steps (1) selection of a **catalyst** from a generation using a numeric **random generator** and then the selection of the second **catalyst** from the same generation using >1 numeric **random generator** with a probability [Wi = [(.sum.j)-i]/.sum.j; the both limits are from j = 1 to n; j, i = rang order of the **catalysts** in a generation sorted by decreasing **catalytic** performance; n = no. of the **catalysts** in a generation]; (2) selection of a component, which is present in the both **catalysts** selected in the step 1, using a numeric **random generator**; and (3) mutation of the **catalysts** by addn. of the component selected in the step 2 to a **catalyst** which does not contain the component and by removal of the component from the **catalyst** which already contains the component. The steps 1-3 were repeated to give 5-50 **catalyst** generations. The new **catalysts** oxidized propane to propene with O2 in an yield of .ltoreq.9%.

L22 ANSWER 7 OF 56 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2002633305 MEDLINE
DOCUMENT NUMBER: 22269934 PubMed ID: 12361984
TITLE: **Combinatorial** mutagenesis to restrict amino acid usage in an enzyme to a reduced set.
AUTHOR: Akanuma Satoshi; Kigawa Takanori; Yokoyama Shigeyuki
CORPORATE SOURCE: RIKEN Genomic Sciences Center, Tsurumi, Yokohama 230-0045, Japan.
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (2002 Oct 15) 99 (21) 13549-53.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

Search completed by David Schreiber 308-4292

FILE SEGMENT: Priority Journals
ENTRY MONTH: 200212
ENTRY DATE: Entered STN: 20021024
Last Updated on STN: 20030105
Entered Medline: 20021204

AB We developed an effective strategy to restrict the amino acid usage in a relatively large protein to a reduced set with conservation of its in vivo function. The 213-residue Escherichia coli orotate phosphoribosyltransferase was subjected to 22 cycles of segment-wise **combinatorial** mutagenesis followed by 6 cycles of site-directed **random** mutagenesis, both coupled with a growth-related phenotype selection. The enzyme eventually tolerated 73 amino acid substitutions: In the final variant, 9 amino acid types (A, D, G, L, P, R, T, V, and Y) occupied 188 positions (88%), and none of 7 amino acid types (C, H, I, M, N, Q, and W) appeared. Therefore, the **catalytic** function associated with a relatively large protein may be achieved with a subset of the 20 amino acid. The converged sequence also implies simpler constituents for proteins in the early stage of **evolution**.

L22 ANSWER 8 OF 56 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 2002:677169 SCISEARCH
THE GENUINE ARTICLE: 580CR
TITLE: Directed **evolution** of selective enzymes and hybrid **catalysts**
AUTHOR: Reetz M T (Reprint)
CORPORATE SOURCE: Max Planck Inst Kohlenforsch, Kaiser Wilhelm Pl 1, D-45470 Mulheim, Germany (Reprint); Max Planck Inst Kohlenforsch, D-45470 Mulheim, Germany
COUNTRY OF AUTHOR: Germany
SOURCE: TETRAHEDRON, (5 AUG 2002) Vol. 58, No. 32, pp. 6595-6602. Publisher: PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, ENGLAND. ISSN: 0040-4020.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 84
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The methods of directed **evolution**, developed in the 1990s, can be applied successfully to the creation of enantioselective enzymes for use in synthetic organic chemistry. The **combination** of appropriate molecular biological methods for **random** mutagenesis and expression coupled with high-throughput screening systems for the determination of ee-values forms the basis of this novel approach to asymmetric **catalysis**. The principle is illustrated by the dramatic enhancement of enantioselectivity of a lipase as the **catalyst** in the hydrolytic kinetic resolution of a chiral ester, the selectivity factor improving from E=1.1 to E=51. Reversal of enantioselectivity is also possible. Finally, the concept of directed **evolution** of selective hybrid **catalysts** has been delineated. (C) 2002 Elsevier Science Ltd. All rights reserved.

L22 ANSWER 9 OF 56 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 2002:523220 HCAPLUS
DOCUMENT NUMBER: 137:310551
TITLE: Second-**generation** MS-based high-throughput screening system for enantioselective **catalysts** and biocatalysts
AUTHOR(S): Schrader, Wolfgang; Eipper, Andreas; Pugh, D. Jonathan; Reetz, Manfred T.

Search completed by David Schreiber 308-4292

CORPORATE SOURCE: Max-Planck-Institut fur Kohlenforschung, Mulheim/Ruhr, D-45470, Germany
SOURCE: Canadian Journal of Chemistry (2002), 80(6), 626-632
CODEN: CJCHAG; ISSN: 0008-4042
PUBLISHER: National Research Council of Canada
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A high-throughput method is described, where the enantioselectivity of approx. 10,000 **catalysts** or biocatalysts can be detd. per day. The method is based on electrospray mass spectrometric techniques using an eight-channel multiplexed (MUX) sprayer system connected to a time-of-flight mass spectrometer. The inlet of the ion source is controlled by a stepping rotor that is continuously moving from one sprayer to the next with a recording time of 100 ms for each channel and a delay time of 50 ms, thus allowing a spectrum to be obtained from each channel every 1.2 s. One cycle, where eight samples are being sprayed in parallel, requires around 70 s, which allows a 96-well microtiter plate to be screened in 14 min. Integration of two pseudo-enantiomers (S)-glycidyl Ph ether and (R)-D5-glycidyl Ph ether is necessary to quantify the enantiomeric excess (ee-value), where one enantiomer is isotopically labeled to allow easy identification of the mass spectrometric signals. Errors of .apprx.2% for the ee-values indicate that in addn. to the significant improvement in sample throughput this is also a precise method for high-throughput screening. This second-**generation** assay is useful for **combinatorial** enantioselective transition-metal **catalysis** and in the directed **evolution** of enantioselective enzymes.

REFERENCE COUNT: 75 THERE ARE 75 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 10 OF 56 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 2002:968477 SCISEARCH
THE GENUINE ARTICLE: 619XP
TITLE: Verification of a novel NADH-binding motif: **Combinatorial** mutagenesis of three amino acids in the cofactor-binding pocket of Corynebacterium 2,5-diketo-D-gluconic acid reductase
AUTHOR: Banta S; Anderson S (Reprint)
CORPORATE SOURCE: Rutgers State Univ, Dept Biochem & Mol Biol, Ctr Adv Biotechnol & Med, 679 Hoes Lane, Piscataway, NJ 08854 USA (Reprint); Rutgers State Univ, Dept Biochem & Mol Biol, Ctr Adv Biotechnol & Med, Piscataway, NJ 08854 USA; Rutgers State Univ, Dept Chem & Biochem Engn, Ctr Adv Biotechnol & Med, Piscataway, NJ 08854 USA
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF MOLECULAR EVOLUTION, (DEC 2002) Vol. 55, No. 6, pp. 623-631.
Publisher: SPRINGER-VERLAG, 175 FIFTH AVE, NEW YORK, NY 10010 USA.
ISSN: 0022-2844.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 23
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB A screening method has been developed to support randomized mutagenesis of amino acids in the cofactor-binding pocket of the NADPH-dependent 2,5-diketo-D-gluconic acid (2,5-DKG) reductase. Such an approach could enable the isolation of an enzyme that can better **catalyze** the reduction of 2,5-DKG to 2-keto-L-gulonic acid (2-KLG) using NADH as a

cofactor. 2-KLG is a valuable precursor to ascorbic acid, or vitamin C, and an enzyme with increased activity with NADH may be able to improve two potential vitamin C production processes. Previously we have identified three amino acid residues that can be **mutated** to improve activity with NADH as a cofactor. As a pilot study to show feasibility, a library was made with these three amino acids randomized, and 300 **random** colonies were screened for increased NADH activity. The activities of seven mutants with apparent improvements were verified using activity-stained native gels, and sequencing showed that the amino acids obtained were similar to some of those already discovered using rational design. The four most active mutants were purified and kinetically characterized. All of the new **mutations** resulted in apparent k(cat) values that were equal to or higher than that of the best mutant obtained through rational design. At saturating levels of cofactor, the best mutant obtained was almost twice as active with NADH as a cofactor as the wild-type enzyme is with NADPH. This screen is a valuable tool for improving 2,5-DKG reductase, and it could easily be modified for improving other aspects of this protein or similar enzymes.

L22 ANSWER 11 OF 56 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 2002:65526 SCISEARCH
THE GENUINE ARTICLE: 511KN
TITLE: High throughput assay for cytochrome P450BM3 for screening libraries of substrates and **combinatorial** mutants
AUTHOR: Tsotsou G E; Cass A E G; Gilardi G (Reprint)
CORPORATE SOURCE: Univ London Imperial Coll Sci Technol & Med, Dept Biol Sci, Biochem Bldg, London SW7 2AY, England (Reprint); Univ London Imperial Coll Sci Technol & Med, Dept Biol Sci, London SW7 2AY, England
COUNTRY OF AUTHOR: England
SOURCE: BIOSENSORS & BIOELECTRONICS, (JAN 2002) Vol. 17, No. 1-2, pp. 119-131.
Publisher: ELSEVIER ADVANCED TECHNOLOGY, OXFORD FULFILLMENT CENTRE THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND.
ISSN: 0956 5663.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 40

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB A rapid method for identifying compounds that are potential substrates for the drug metabolising enzyme cytochrome P450 is described. The strategy is based on the detection of a degradation product of NAD(P)H oxidation during substrate turnover by the enzyme expressed in Escherichia coli cells spontaneously lysed under the experimental conditions. The performance of the method has been tested on two known substrates of the wild-type cytochrome P450 BM3, arachidonic (AA) and lauric (LA) acids, and two substrates with environmental significance, the anionic surfactant sodium dodecyl sulfate (SDS), and the solvent 1, 1,2,2-tetrachloroethane (TCE). The minimal background signal given from cells expressing cytochrome P450 BM3 in the absence of added substrate is only 3% of the signal in the presence of saturating substrate. Control experiments have proven that this method is specifically detecting NADPH oxidation by **catalytic** turnover of P450 BM3. The assay has been adapted to a microtitre plate format and used to screen a series of furazan derivatives as potential substrates. Three derivatives were identified as substrates. The method gave a significant different signal for two isomeric furazan derivatives. All results found on the cell lysate were verified and

confirmed with the purified enzyme. This strategy opens the way to automated high throughput screening of NAD(P)H-linked enzymatic activity of molecules of pharmacological and biotechnological interest and libraries of **random** mutants of NAD(P) H -dependent biocatalysts.
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L22 ANSWER 12 OF 56 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2002311013 MEDLINE
DOCUMENT NUMBER: 22050811 PubMed ID: 12054768
TITLE: An ensemble of theta class glutathione transferases with novel **catalytic** properties generated by **stochastic recombination** of fragments of two mammalian enzymes.
AUTHOR: Broo Kerstin; Larsson Anna-Karin; Jemth Per; Mannervik Bengt
CORPORATE SOURCE: Department of Biochemistry, Uppsala University, Biomedical Center, Box 576, SE-751 23 Uppsala, Sweden.
SOURCE: JOURNAL OF MOLECULAR BIOLOGY, (2002 Apr 19) 318 (1) 59-70. Journal code: 2985088R. ISSN: 0022-2836.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200207
ENTRY DATE: Entered STN: 20020611
Last Updated on STN: 20020713
Entered Medline: 20020712

AB The correlation between sequence diversity and enzymatic function was studied in a library of Theta class glutathione transferases (GSTs) obtained by **stochastic recombination** of fragments of cDNA encoding human GST T1-1 and rat GST T2-2. In all, 94 randomly picked clones were characterized with respect to sequence, expression level, and **catalytic** activity in the conjugation reactions between glutathione and six alternative electrophilic substrates. Out of these six different compounds, dichloromethane is a selective substrate for human GST T1-1, whereas 1-menaphthyl sulfate and 1-chloro-2,4-dinitrobenzene are substrates for rat GST T2-2. The other three substances serve as substrates for both enzymes. Through this broad characterization, we have identified enzyme variants that have acquired novel activity profiles that differ substantially from those of the original GSTs. In addition, the expression levels of many clones were improved in comparison to the parental enzyme. A library of mutants can thus display a distribution of properties from which highly divergent **evolutionary** pathways may emerge, resembling natural **evolutionary** processes. From the GST library, a clone was identified that, by the point **mutation** N49D in the rat GST T2-2 sequence, has a 1700% increased activity with 1-menaphthyl sulfate and a 60% decreased activity with 4-nitrophenethyl bromide. Through the N49D **mutation**, the ratio of these activities has thus been altered 40-fold. An extensive characterization of a population of **stochastically mutated** enzymes can accordingly be used to find variants with novel substrate-activity profiles and altered **catalytic** properties. Recursive **recombination** of selected sequences displaying optimized properties is a strategy for the engineering of proteins for medical and biochemical applications. Such sequential design is **combinatorial** protein chemistry based on remodeling of existing **structural** scaffolds and has similarities to **evolutionary** processes in nature.
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Search completed by David Schreiber 308-4292

Zhou 09/909,038

L22 ANSWER 13 OF 56 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:636273 HCAPLUS
DOCUMENT NUMBER: 135:176420
TITLE: Methods for generating enzymes using nucleic acid-protein fusion approaches
INVENTOR(S): Kurz, Markus; Lohse, Peter
PATENT ASSIGNEE(S): Phylos, Inc., USA
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001062983	A1	20010830	WO 2001-US6147	20010226
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2001024789	A1	20010927	US 2001-795037	20010226
EP 1266035	A1	20021218	EP 2001-916243	20010226
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003523756	T2	20030812	JP 2001-561791	20010226

PRIORITY APPLN. INFO.: US 2000-184515P P 20000224
WO 2001-US6147 W 20010226

AB Disclosed herein are novel methods for the **generation** and identification of **catalytic** and autoproteolytic proteins (enzymes) using nucleic acid-protein fusion approaches. In a first aspect, the invention features a method that involves the steps of: (a) providing a candidate **catalytic** protein fusion mol., including a candidate **catalytic** protein linked to both its nucleic acid coding sequence and a substrate; and (b) detg. whether the candidate **catalytic** protein **catalyzes** a reaction of the substrate by assaying for an alteration in mol. size, charge, or conformation of the fusion mol., relative to an unreacted fusion mol., thereby identifying a nucleic acid mol. which encodes a **catalytic** protein. The alteration in mol. size, charge, or conformation of the reacted fusion mol. may be detected by an alteration in electrophoretic mobility or by column chromatog. (for example, by HPLC, FPLC, ion exchange column chromatog., or size exclusion chromatog. anal.). In a related aspect, the invention features another method for identifying a nucleic acid mol. which encodes a **catalytic** protein, the method involving the steps of: (a) providing a candidate **catalytic** protein fusion mol., including a candidate **catalytic** protein linked to both its nucleic acid coding sequence and a substrate; (b) allowing the candidate **catalytic** protein to **catalyze** a reaction of the substrate in soln.; (c) contacting the product of step (b) with a capture mol. that has specificity for and binds a reacted fusion mol., but not an unreacted fusion mol., the capture mol. being immobilized on a solid support; and (d) detecting the reacted fusion mol. in assocn. with the

Search completed by David Schreiber 308-4292

solid support, thereby identifying a nucleic acid mol. which encodes a **catalytic** protein. In a third aspect, the invention features yet another method for identifying a nucleic acid mol. which encodes a **catalytic** protein, the method involving the steps of: (a) providing a candidate **catalytic** protein fusion mol., including a candidate **catalytic** protein linked to both its nucleic acid coding sequence and a substrate, the substrate being covalently bonded to an affinity tag; (b) allowing the candidate **catalytic** protein to **catalyze** a reaction of the substrate in soln.; (c) contacting the product of step (b) with a capture mol. that is specific for the affinity tag, the capture mol. being immobilized on a solid support; and (d) detg. whether the fusion mol. is bound to the solid support, wherein the detn. that a fusion mol. is not bound to the solid support identifies a nucleic acid mol. which encodes a **catalytic** protein. In a fourth aspect, the invention features a further method for identifying a nucleic acid mol. which encodes a **catalytic** protein, the method involving the steps of: (a) providing a candidate **catalytic** protein fusion mol., including a candidate **catalytic** protein linked to both its nucleic acid coding sequence and a substrate; (b) allowing the candidate **catalytic** protein to **catalyze** a reaction of the substrate in soln. in the presence of an affinity tag, the reaction resulting in the covalent attachment of the affinity tag to the fusion mol.; (c) immunopptg. the product of step (b) with an antibody that is specific for the affinity tag; and (d) detecting the immunopptn. complex, thereby identifying the fusion mol. as having a nucleic acid mol. which encodes a **catalytic** protein. These methods may be used for the isolation of novel enzymes with tailor-made activities and substrate specificities from randomized peptide and protein libraries, or for the directed **evolution** of existing enzymes with improved **catalytic** features.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 14 OF 56 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:618279 HCAPLUS
DOCUMENT NUMBER: 135:177723
TITLE: Computationally targeted **evolutionary** design
INVENTOR(S): Voigt, Christopher; Mayo, Stephen L.; Arnold, Frances H.; Wang, Zhen-Gang
PATENT ASSIGNEE(S): California Institute of Technology, USA
SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001061344	A1	20010823	WO 2001-US5043	20010216

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

Search completed by David Schreiber 308-4292

US 2001051855 A1 20011213 US 2001-795500 20010216
PRIORITY APPLN. INFO.: US 2000-183171P P 20000217
AB The invention relates to improved methods for directed **evolution** of polymers, including directed **evolution** of nucleic acids and proteins. Specifically, the methods of the invention include anal. methods for identifying "**structurally** tolerant" residues of a polymer. **Mutations** of these, **structurally** tolerant residues are less likely to adversely affect desirable properties of a polymer sequence. The invention further provides improved methods for directed **evolution** wherein the **structurally** tolerant residues of a polymer are selectively **mutated**. Computer systems for implementing anal. methods of the invention are also provided.
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 15 OF 56 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:519380 HCAPLUS
DOCUMENT NUMBER: 135:119237
TITLE: Protein selection using RNA-protein fusions in the presence of high salt
INVENTOR(S): Szostak, Jack W.; Roberts, Richard W.; Liu, Rihe
PATENT ASSIGNEE(S): General Hospital Corp., USA
SOURCE: U.S., 55 pp., Cont.-in-part of U.S. Ser. No. 7,005.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6261804	B1	20010717	US 1999-247190	19990209
US 6258558	B1	20010710	US 1998-7005	19980114
ZA 9800489	A	19980908	ZA 1998-489	19980121
US 6518018	B1	20030211	US 1999-238710	19990128
US 6214553	B1	20010410	US 1999-244794	19990205
US 6281344	B1	20010828	US 1999-244796	19990205
US 6207446	B1	20010327	US 1999-430049	19991029
WO 2000047775	A1	20000817	WO 2000-US2589	20000201
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1151143	A1	20011107	EP 2000-913326	20000201
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NZ 513153	A	20030328	NZ 2000-513153	20000201
US 2003022236	A1	20030130	US 2001-876235	20010606
NO 2001003842	A	20011002	NO 2001-3842	20010807

PRIORITY APPLN. INFO.:
US 1997-35963P P 19970121
US 1997-64491P P 19971106
US 1998-7005 A2 19980114
US 1999-247190 A 19990209
WO 2000-US2589 W 20000201

Search completed by David Schreiber 308-4292

Zhou 09/909,038

AB The purpose of the present invention is to allow the principles of in vitro selection and in vitro **evolution** to be applied to proteins. The invention facilitates the isolation of proteins with desired properties from large pools of partially or completely **random** amino acid sequences. In addn., the invention solves the problem of recovering and amplifying the protein sequence information by covalently attaching the mRNA coding sequence to the protein mol. In general, the inventive method consists of an in vitro or in situ transcription/translation protocol that generates protein covalently linked to the 3' end of its own mRNA, i.e., an RNA-protein fusion. This is accomplished by synthesis and in vitro or in situ translation of an mRNA mol. with a peptide acceptor attached to its 3' end. One preferred peptide acceptor is puromycin, a nucleoside analog that adds to the C-terminus of a growing peptide chain and terminates translation. In one preferred design, a DNA sequence is included between the end of the message and the peptide acceptor which is designed to cause the ribosome to pause at the end of the open reading frame, providing addnl. time for the peptide acceptor (for example, puromycin) to accept the nascent peptide chain before hydrolysis of the peptidyl-tRNA linkage. If desired, the resulting RNA-protein fusion allows repeated rounds of selection and amplification because the protein sequence information may be recovered by reverse transcription and amplification (for example, by PCR amplification as well as any other amplification technique, including RNA-based amplification techniques such as 3SR or TSA). The amplified nucleic acid may then be transcribed, modified, and in vitro or in situ translated to generate mRNA-protein fusions for the next round of selection. The ability to carry out multiple rounds of selection and amplification enables the enrichment and isolation of very rare mols., e.g., one desired mol. out of a pool of 1015 members. This in turn allows the isolation of new or improved proteins which specifically recognize virtually any target or which **catalyze** desired chem. reactions. In a related aspect, the invention features methods for producing libraries (for example, protein, DNA, or RNA-fusion libraries) or methods for selecting desired mols. (for example, protein, DNA, or RNA mols. or mols. having a particular function or altered function) which involve a step of posttranslational incubation in the presence of high salt (including, without limitation, high salt which includes a monovalent cation, such as K.sup.+, NH4.sup.+, or Na.sup.+, a divalent cation, such as Mg.sup.+2, or a **combination** thereof). This incubation may be carried out at approx. room temp. or approx. -20.degree.. and preferred salt concns. of between approx. 125 mM-1.5 M (more preferably, between approx. 300 mM-600 mM) for monovalent cations and between approx. 25 mM-200 mM for divalent cations. In another related aspect, the invention features kits for carrying out any of the selection methods described herein. In a third and final aspect, the invention features a microchip that includes an array of immobilized single-stranded nucleic acids, the nucleic acids being hybridized to RNA-protein fusions. Preferably, the protein component of the RNA-protein fusion is encoded by the RNA. The selection systems of the present invention have com. applications in any area where protein technol. is used to solve therapeutic, diagnostic, or industrial problems. This selection technol. is useful for improving or altering existing proteins as well as for isolating new proteins with desired functions. These proteins may be naturally-occurring sequences, may be altered forms of naturally-occurring sequences, or may be partly or fully synthetic sequences. In addn., these methods may also be used to isolate or identify useful nucleic acid or small mol. targets. To develop the present methodol., RNA-protein fusions were initially generated using highly simplified mRNA templates contg. 1-2 codons. Exemplary fusions were also generated which contained, within the protein portion, the

epitope tag for the c-myc monoclonal antibody 9E10.
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 16 OF 56 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 2001:584812 SCISEARCH
THE GENUINE ARTICLE: 452AQ
TITLE: Selection of enantioselective acyl transfer **catalysts** from a pooled peptide library through a fluorescence-based activity assay: An approach to kinetic resolution of secondary alcohols of broad **structural** scope
AUTHOR: Copeland G T; Miller S J (Reprint)
CORPORATE SOURCE: Boston Coll, Merkert Chem Ctr, Dept Chem, Chestnut Hill, MA 02467 USA (Reprint)
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, (11 JUL 2001) Vol. 123, No. 27, pp. 6496-6502.
Publisher: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036 USA.
ISSN: 0002-7863.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 42
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB An assay employing a fluorescently labeled split and pool peptide library has been applied to the discovery of a new class of octapeptide **catalysts** for the kinetic resolution of secondary alcohols. A highly diverse library of peptide-based **catalysts** was synthesized on solid-phase synthesis beads such that each individual bead was co-functionalized with (i) a uniform loading of a pH-sensitive fluorophore and () a unique peptide-based **catalyst**. The library was then screened for activity in acylation reactions employing (+/-)-sec-phenylethanol as the substrate and acetic anhydride as the acylation agent. From the most active **catalysts**, a lead peptide (4) was identified that provides a selectivity-factor (k(rel)) of 8.2 upon resynthesis and evaluation under homogeneous conditions. A "directed" second-**generation** split and pool peptide library was synthesized such that the new peptide sequences in the library were biased toward the lead **structure. Random** samples of the second **generation** library were screened in single bead assays that revealed several new peptide-based **catalysts** that afford improved selectivities in kinetic resolutions. Peptide **catalyst** 13 proves effective for the kinetic resolution of sec-phenylethanol (k(rel) = 20), as well as eight other secondary alcohols of a broad substrate scope (k(rel) = 4 to > 50).

L22 ANSWER 17 OF 56 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:149778 HCAPLUS
DOCUMENT NUMBER: 134:322646
TITLE: Probing Functional Perfection in Substructures of Ribonuclease T1: Double **Combinatorial Random** Mutagenesis Involving Asn43, Asn44, and Glu46 in the Guanine Binding Loop
AUTHOR(S): Kumar, Kapil; Walz, Frederick G., Jr.
CORPORATE SOURCE: Department of Chemistry, Kent State University, Kent, OH, 44242, USA
SOURCE: Biochemistry (2001), 40(12), 3748-3757
CODEN: BICHAW; ISSN: 0006-2960

Search completed by David Schreiber 308-4292

PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Combinatorial random** mutagenesis involving either Asn43 with Asn44 (set 1) or Glu46 with an adjacent insertion (set 2) were undertaken to explore the functional perfection of the guanine recognition loop of RNase T1 (RNase T1). Four hundred unique **recombinants** were screened in each set for their ability to enhance enzyme **catalysis** of RNA cleavage. After a thorough selection procedure, only six variants were found that were either as active or more active than wild type which included substitutions of Asn43 by Gly, His, Leu, or Thr, an unplanned Tyr45Ser substitution and Glu46Pro with an adjacent Glu47 insertion. Asn43His-RNase T1 has the same loop sequence as that for RNases Pb1 and F12. None of the most active mutants were single substitutions at Asn44 or double substitutions at Asn43 and Asn44. A total of 13 variants were purified, and these were subjected to kinetic anal. using RNA, GpC, and ApC as substrates. Modestly enhanced activities with GpC and RNA involved both kcat and KM effects. Mutants having low activity with GpC had proportionately even lower relative activity with RNA. Asn43Gly-RNase T1 and all five of the purified mutants in set 2 exhibited similar values of kcat/KM for ApC which were the highest obsd. and about 10-fold that for wild type. The specificity ratio [(kcat/KM)GpC/(kcat/KM)ApC] varied over 30 000-fold including a 10-fold increase [Asn43His variant; mainly due to a low (kcat/KM)ApC] and a 3000-fold decrease (Glu46Ser/(insert)Gly47 variant; mainly due to a low (kcat/KM)GpC) as compared with wild type. It is interesting that kcat (GpC) for the Tyr45Ser variant was almost 4-fold greater than for wild type and that Pro46/(insert)Glu47 RNase T1 is 70-fold more active than the permuted variant (insert)Pro47-RNase T1 which has a conserved Glu46. In any event, the observation that only 6 out of 800 variants surveyed had wild-type activity supports the view that functional perfection of the guanine recognition loop of RNase T1 has been achieved.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 18 OF 56 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 2001636115 MEDLINE
DOCUMENT NUMBER: 21543697 PubMed ID: 11688718
TITLE: The **stochastic evolution** of **catalysts** in spatially resolved molecular systems.
AUTHOR: Mccaskill J S; Fuchslin R M; Altmeyer S
CORPORATE SOURCE: GMD, National Research Center for Information Technology, St Augustin, Germany.
SOURCE: BIOLOGICAL CHEMISTRY, (2001 Sep) 382 (9) 1343-63. Journal code: 9700112. ISSN: 1431-6730.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200203
ENTRY DATE: Entered STN: 20011105
Last Updated on STN: 20020320
Entered Medline: 20020319

AB A fully **stochastic** chemical modelling technique is derived which describes the influence of spatial separation and discrete population size on the **evolutionary** stability of coupled amplification in biopolymers. The model is analytically tractable for an infinite-dimensional space (simplex geometry), which also provides insight into **evolution** in normal Euclidean space. The results are

compared with **stochastic** simulations describing the co-**evolution** of **combinatorial** families of molecular sequences both in the simplex geometry and in lower (one, two and three) space dimensions. They demonstrate analytically the generic limits which exploitation place on co-evolving multi-component amplification systems. In particular, there is an optimal diffusion (or migration) coefficient for cooperative amplification and minimal and maximal threshold values for stable cooperation. Over a bounded range of diffusion rates, the model also exhibits stable limit cycles. Furthermore, the co-operatively coupled system has a maximum tolerable error rate at intermediate rates of diffusion. A tractable model is thereby established which demonstrates that spatial effects can stabilize **catalytic** biological information. The analytic behaviour in infinite-dimensional simplex space is seen to provide a reasonable guide to the spatial dependence of the error threshold in physical space. Nanoscale possibilities for the **evolution** of **catalysis** on the basis of the model are outlined. We denote the modelling technique by PRESS, Probability Reduced **Evolution** of Spatially-discrete Species.

L22 ANSWER 19 OF 56 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 2001:471106 SCISEARCH
THE GENUINE ARTICLE: 438YK
TITLE: In vitro abzyme **evolution** to optimize antibody recognition for **catalysis**
AUTHOR: Takahashi N; Kakinuma H; Liu L D; Nishi Y; Fujii I (Reprint)
CORPORATE SOURCE: Biomol Engn Res Inst, 6-2-3 Furuedai, Suita, Osaka 5650784, Japan (Reprint); Biomol Engn Res Inst, Suita, Osaka 5650784, Japan; Japan Tobacco Inc, Lab Life Sci & Biomed Engn, Aoba Ku, Yokohama, Kanagawa 2278512, Japan
COUNTRY OF AUTHOR: Japan
SOURCE: NATURE BIOTECHNOLOGY, (JUN 2001) Vol. 19, No. 6, pp. 563-567.
Publisher: NATURE AMERICA INC, 345 PARK AVE SOUTH, NEW YORK, NY 10010-1707 USA.
ISSN: 1087-0156.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 30

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Enzymes have evolved their ability to use binding energies for **catalysis** by increasing the affinity for the transition state of a reaction and decreasing the affinity for the ground state. To evolve abzymes toward higher **catalytic** activity, we have reconstructed an enzyme-**evolutionary** process in vitro. Thus, a phage-displayed **combinatorial** library from a hydrolytic abzyme, 6D9, generated by the conventional in vivo method with immunization of the transition-state analog (TSA), was screened against a newly devised TSA to optimize the differential affinity for the transition state relative to the ground state. The library format successfully afforded evolved variants with 6- to 20-fold increases in activity (k(cat)) as compared with 6D9. Structural analysis revealed an advantage of the in vitro **evolution** over the in vivo **evolution**: an induced **catalytic** residue in the evolved abzyme arises from double mutations in one codon, which rarely occur in somatic hypermutation in the immune response.

L22 ANSWER 20 OF 56 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2001262840 MEDLINE
DOCUMENT NUMBER: 21230545 PubMed ID: 11333020

Search completed by David Schreiber 308-4292

TITLE: The effect of cytidine on the **structure** and function of an RNA ligase ribozyme.
AUTHOR: Rogers J; Joyce G F
CORPORATE SOURCE: Department of Chemistry, The Scripps Research Institute, La Jolla, California 92037, USA.
SOURCE: RNA, (2001 Mar) 7 (3) 395-404.
Journal code: 9509184. ISSN: 1355-8382.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010521
Last Updated on STN: 20010521
Entered Medline: 20010517

AB A cytidine-free ribozyme with RNA ligase activity was obtained by in vitro **evolution**, starting from a pool of **random**-sequence RNAs that contained only guanosine, adenosine, and uridine. This ribozyme contains 74 nt and **catalyzes** formation of a 3',5'-phosphodiester linkage with a **catalytic** rate of 0.016 min(-1). The RNA adopts a simple secondary **structure** based on a three-way junction motif, with ligation occurring at the end of a stem region located several nucleotides away from the junction. Cytidine was introduced to the cytidine-free ribozyme in a **combinatorial** fashion and additional rounds of in vitro **evolution** were carried out to allow the molecule to adapt to this added component. The resulting cytidine-containing ribozyme formed a 3',5' linkage with a **catalytic** rate of 0.32 min(-1). The improved rate of the cytidine-containing ribozyme was the result of 12 **mutations**, including seven added cytidines, that remodeled the internal bulge loops located adjacent to the three-way junction and stabilized the peripheral stem regions.

L22 ANSWER 21 OF 56 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:87221 HCAPLUS
DOCUMENT NUMBER: 134:295384
TITLE: **Combinatorial** and **evolution**-based methods in the creation of enantioselective **catalysts**
AUTHOR(S): Reetz, Manfred T.
CORPORATE SOURCE: Max-Planck-Institut fur Kohlenforschung, Mulheim an der Ruhr, 45470, Germany
SOURCE: Angewandte Chemie, International Edition (2001), 40(2), 284-310
CODEN: ACIEF5; ISSN: 1433-7851
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with at least 102 refs. discusses the development of techniques for the **generation** and evaluation of enantioselective **catalysts**. The directed **evolution** of enzymes and the **combinatorial generation** of enantioselective metal **catalysts** are discussed. High-throughput screening techniques for the evaluation of enantioselective **catalysts** are also discussed.

REFERENCE COUNT: 236 THERE ARE 236 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 22 OF 56 HCAPLUS COPYRIGHT 2003 ACS on STN

Search completed by David Schreiber 308-4292

Zhou 09/909,038

ACCESSION NUMBER: 2001:59125 HCAPLUS
DOCUMENT NUMBER: 134:248639
TITLE: **Combinatorial** and computational challenges for biocatalyst design
AUTHOR(S): Arnold, Frances H.
CORPORATE SOURCE: Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, CA, 91125, USA
SOURCE: Nature (London) (2001), 409(6817), 253-257
CODEN: NATUAS; ISSN: 0028-0836
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with 45 refs. Nature provides a fantastic array of **catalysts** extremely well suited to supporting life, but usually not so well suited for technol. Whether biocatalysis will have a significant technol. impact depends on our finding robust routes for tailoring nature's catalysts or redesigning them anew. Lab. **evolution** methods are now used widely to fine-tune the selectivity and activity of enzymes. The current rapid development of these **combinatorial** methods promises solns. to more complex problems, including the creation of new biosynthetic pathways. Computational methods are also developing quickly. The marriage of these approaches will allow us to **generate** the efficient, effective **catalysts** needed by the pharmaceutical, food and chems. industries and should open up new opportunities for producing energy and chems. from renewable resources.
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 23 OF 56 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:640547 HCAPLUS
TITLE: Exploring the trade-off between constitutional diversity and **combinatorial** opportunity in the **evolution** of nucleic-acid-based **catalytic** function
AUTHOR(S): Joyce, Gerald F.
CORPORATE SOURCE: Departments of Chemistry and Molecular Biology, The Scripps Research Institute, La Jolla, CA, 92037, USA
SOURCE: Abstracts of Papers, 222nd ACS National Meeting, Chicago, IL, United States, August 26-30, 2001 (2001), ORGN-184. American Chemical Society: Washington, D. C.
CODEN: 69BUZP
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB In considering the **catalytic** potential of RNA, esp. in relation to proteins, one is struck by the limited range of functional groups that exist among the four nucleotides. DNA, lacking a 2'-hydroxyl group, would seem to be even more functionally impoverished than RNA. Terrestrial biol. apparently never had the opportunity or incentive to invent DNA enzymes, although this has been accomplished in the lab. through in vitro **evolution**. One such DNA enzyme is the "10-23" motif, which can be made to cleave almost any RNA substrate in a sequence-specific manner, with a **catalytic** efficiency exceeding that of all known RNA enzymes. Another, more complex DNA enzyme is the "10-28" motif, which **catalyzes** the site-specific depurination of DNA with a **catalytic** rate enhancement of about 106-fold. Can enzymes be obtained from building blocks that have even less constitutional diversity

Search completed by David Schreiber 308-4292

than the four nucleotides Starting from a mol. that contained roughly equal proportions of all four nucleotides, in vitro **evolution** was used to obtain an RNA ligase ribozyme that lacks cytidine. This mol. folds into a defined **structure** and exhibits a **catalytic** rate enhancement of about 105-fold. Another cytidine-free ligase ribozyme was obtained starting from a pool of **random**-sequence RNAs that contained only guanosine, adenosine, and uridine. This in turn was used to develop a ligase ribozyme that contains only two distinct building blocks, yet achieves a **catalytic** rate enhancement of about 104-fold. This work demonstrates that **evolution** can cope with a very restricted set of chem. building blocks in generating macromols. that have a complex **structure** and function.

L22 ANSWER 24 OF 56 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:196917 HCAPLUS
TITLE: Application of **combinatorial** chemistry and biology for the **generation** of enzymes and enzyme-like **catalysts**
AUTHOR(S): Tawfik, Dan S.
CORPORATE SOURCE: MRC Centre for Protein Engineering, Cambridge University, Cambridge CB2 2QH, UK
SOURCE: Abstracts of Papers - American Chemical Society (2001), 221st, AGFD-098
CODEN: ACSRAL; ISSN: 0065-7727
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; Meeting Abstract
LANGUAGE: English
AB Enzymes - nature's **catalysts** - exhibit remarkable rate accelerations and specificity of action. They offer an economical, environmentally-friendly alternative to man-made chem. **catalysts** . Albeit, enzymes evolved to meet the needs of natural organisms and therefore require altering, or even the making novel ones, to fit the needs of man-made processes. I will describe the application of **combinatorial** chem. for the synthesis and screening of polymeric enzyme-like **catalysts** - synzymes - generated by the modification of polyethyleneiminine. These synzymes exhibit rate accelerations as high as 106 and are resistant to both extreme pHs and high temps. I will also describe a novel approach for the directed **evolution** of enzymes applying in vitro compartmentalisation (in water-in-oil emulsions) to select very large gene pools (.apprx.1010) for genes encoding proteins with enzymic (and binding) activities. Uniquely, selection is performed entirely in vitro (no cloning or transformation is required) for the formation of the desirable product and turnover.

L22 ANSWER 25 OF 56 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:749680 HCAPLUS
DOCUMENT NUMBER: 136:364231
TITLE: **Combinatorial** creation of oligonucleotides with various molecular functions by molecular **evolution** engineering and their application as devices
AUTHOR(S): Nogawa, Masayuki; Ito, Yoshihiro
CORPORATE SOURCE: Department of Engineering, Bio-Engineering Course, Tokushima University, Japan
SOURCE: Kagaku (Kyoto, Japan) (2001), 56(10), 64-65
CODEN: KAKYAU; ISSN: 0451-1964
PUBLISHER: Kagaku Dojin
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

Search completed by David Schreiber 308-4292

Zhou 09/909,038

AB A review described **combinatorial** approach to find out useful functional mols. from **random** oligonucleotide libraries by the selection methods based on mol. **evolution** engineering. Ribozymes that **catalyzed** Diels-Alder reaction yielding stereo-specific products were described as examples of the substances found by such **combinatorial** approach. A method that could select ATP-binding aptamer from an RNA library by using fluorescence-labeled UTP was also presented. Use of the ribozymes and/or aptamers for building biosensor array was also described as an example of the application of the **combinatorial** products as devices.

L22 ANSWER 26 OF 56 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 2001:252248 SCISEARCH
THE GENUINE ARTICLE: 413CL
TITLE: Biotechnological applications of phage and cell display
AUTHOR: Benhar I (Reprint)
CORPORATE SOURCE: Tel Aviv Univ, George S Wise Fac Life Sci, Dept Mol Microbiol & Biotechnol, Green Bldg, Room 202, IL-69978 Tel Aviv, Israel (Reprint); Tel Aviv Univ, George S Wise Fac Life Sci, Dept Mol Microbiol & Biotechnol, IL-69978 Tel Aviv, Israel
COUNTRY OF AUTHOR: Israel
SOURCE: BIOTECHNOLOGY ADVANCES, (FEB 2001) Vol. 19, No. 1, pp. 1-33.
Publisher: PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, ENGLAND.
ISSN: 0734-9750.
DOCUMENT TYPE: General Review; Journal
LANGUAGE: English
REFERENCE COUNT: 233
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Tn recent years, the use of surface-display vectors for displaying polypeptides on the surface of bacteriophage and bacteria, **combined** with in vitro selection technologies, has transformed the way in which we generate and manipulate ligands, such as enzymes, antibodies and peptides. Phage display is based on expressing **recombinant** proteins or peptides fused to a phage coat protein. Bacterial display is based on expressing **recombinant** proteins fused to sorting signals that direct their incorporation on the cell surface. In both systems, the generic information encoding for the displayed molecule is physically linked to its product via the displaying particle. Using these two complementary technologies, rye are now able to design repertoires of ligands from scratch and use the power of affinity selection to select those ligands having the desired (biological) properties from a large excess of irrelevant ones. With phage display, tailor-made proteins (fused peptides, antibodies, enzymes, DNA-binding proteins) may be synthesized and selected to acquire the desired **catalytic** properties or affinity of binding and specificity for in vitro and in vivo diagnosis, for immunotherapy of human disease or for biocatalysis. Bacterial surface display has found a range of applications in the expression of various antigenic determinants, heterologous enzymes, single-chain antibodies, and **combinatorial** peptide libraries. This review explains the basis of phage and bacterial surface display and discusses the contributions made by these two leading technologies to biotechnological applications. This review focuses mainly on three areas where phage and cell display have had the greatest impact, namely, antibody engineering, enzyme technology and vaccine development. (C) 2001 Elsevier Science Inc. All rights reserved.

Search completed by David Schreiber 308-4292

L22 ANSWER 27 OF 56 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2001:257120 BIOSIS
DOCUMENT NUMBER: PREV200100257120
TITLE: Application of **combinatorial** chemistry and biology for the **generation** of enzymes and enzyme-like **catalysts.**
AUTHOR(S): Tawfik, Dan S. (1)
CORPORATE SOURCE: (1) MRC Centre for Protein Engineering, Cambridge University, Hills Road, Cambridge, CB2 2QH: dst@mrc-lmb.cam.ac.uk UK
SOURCE: Abstracts of Papers American Chemical Society, (2001) Vol. 221, No. 1-2, pp. AGFD 98. print.
Meeting Info.: 221st National Meeting of the American Chemical Society San Diego, California, USA April 01-05, 2001
ISSN: 0065-7727.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L22 ANSWER 28 OF 56 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:742305 HCAPLUS
DOCUMENT NUMBER: 133:306966
TITLE: In vitro ribosome **evolution** for the formation of non-standard polymer products
INVENTOR(S): Green, D. Rachel
PATENT ASSIGNEE(S): Johns Hopkins University School of Medicine, USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000061815	A1	20001019	WO 2000-US9681	20000412
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6358713	B1	20020319	US 2000-547537	20000412

PRIORITY APPLN. INFO.: US 1999-128848P P 19990412

AB Methods for selecting rRNA variants that **catalyze** formation of non-std. polymers are described. An iterative, in vitro selection system is described that allows for the isolation of variant major rRNAs of large ribosomal subunits with novel properties. The method includes crosslinking a peptidyl substrate to ribosomes, wherein the major RNA of the large ribosomal subunit in a plurality of the ribosomes is an rRNA variant mol. The ribosomes can be eukaryotic or prokaryotic ribosomes, such as Escherichia coli or Bacillus stearothermophilus ribosomes, and the rRNA variant can be a 28S or 23S rRNA variant mol. The crosslinked ribosomes and a labeled, derivatized aminoacyl substrate are reacted under conditions such that the labeled, derivatized aminoacyl substrate is

transferred to the rRNA variant mol. to form labeled ribosomes, and the rRNA variant mols. are selected from labeled ribosomes. Thus, the aminoacyl (A site) tRNA analog 4-thio-dT-p-C-p-puromycin (s4TCPm) photochem. crosslinks with high efficiency and specificity to G2553 of 23S rRNA and is peptidyltransferase-reactive in its crosslinked state, establishing proximity between the highly conserved 2555 loop in domain V of 23S rRNA and the universally conserved CCA end of tRNA. The selection system allows rRNA variants to be isolated with enriched **catalytic** activity on altered peptidyl and aminoacyl ribosome substrates such as D-amino acids, Me phosphinyl derivatized substrates, N-derivatized, and .beta.-amino acid substrates. The coupling of such evolved ribosomes with RNA-peptide fusion technol. allows for the **generation** of **combinatorial** chem. libraries than can be screened and deconvoluted to identify novel and biol. stable target compds. The aminoacyl (A site) tRNA analog 4-thio-dT-p-C-p-puromycin (s4TCPm) photochem. cross-links with high efficiency and specificity to G2553 of 23S rRNA and is peptidyl transferase reactive in its cross-linked state, establishing proximity between the highly conserved 2555 loop in domain V of 23S rRNA and the universally conserved CCA end of tRNA.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 29 OF 56 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:210438 HCAPLUS
DOCUMENT NUMBER: 132:247132
TITLE: Parallel SELEX allowing for asymmetrical reactions in **combinatorial** chemistry of DNA
INVENTOR(S): Eaton, Bruce; Tarasow, Theodore M.
PATENT ASSIGNEE(S): Nexstar Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 109 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 121
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000017398	A1	20000330	WO 1999-US21079	19990913
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6048698	A	20000411	US 1998-157601	19980921
CA 2344288	AA	20000330	CA 1999-2344288	19990913
AU 9960392	A1	20000410	AU 1999-60392	19990913
EP 1115887	A1	20010718	EP 1999-969450	19990913
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002526511	T2	20020820	JP 2000-574297	19990913

PRIORITY APPLN. INFO.:
US 1998-157601 A 19980921
US 1994-309245 A2 19940920
US 1996-618700 A2 19960320
WO 1999-US21079 W 19990913

Search completed by David Schreiber 308-4292

Zhou 09/909,038

AB This invention discloses a method for parallel SELEX (Systematic **Evolution** of Ligands by Exponential enrichment), consisting of prepg. a nucleic acid test mixt., coupling each nucleic acid to a small org. mol., forming a product library via bond formation of the attached org. mols. with free reactant(s) **catalyzed** by their attached nucleic acids, and selecting desired products, both for identification and for amplification of their **catalytic** nucleic acids. In this process, a large nucleic acid test mixt. is provided with each nucleic acid linked to a chem. reactant, premised on the assumption that in the library there will be nucleic acids capable of mediating a reaction between their own attached reactants and some other free reactants. Sepg. the desired products, then, allows for enrichment of their attached **catalytic** nucleic acids. Parallel SELEX can include the formation of product libraries using asym. reactions. Unlike conventional **combinatorial** chem. approaches, the reactions can be included with no knowledge of the stereochem. outcome. Generic examples using the parallel SELEX method are given.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 30 OF 56 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:238004 HCAPLUS
DOCUMENT NUMBER: 132:247140
TITLE: Parallel SELEX allowing for asymmetrical reactions in **combinatorial** chemistry
INVENTOR(S): Eaton, Bruce; Tarasow, Theodore M.
PATENT ASSIGNEE(S): NeXstar Pharmaceuticals, Inc., USA
SOURCE: U.S., 54 pp., Cont.-in-part of U.S. 5,858,660.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 121
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6048698	A	20000411	US 1998-157601	19980921
US 5723289	A	19980303	US 1994-309245	19940920
US 5858660	A	19990112	US 1996-618700	19960320
CA 2344288	AA	20000330	CA 1999-2344288	19990913
WO 2000017398	A1	20000330	WO 1999-US21079	19990913
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9960392	A1	20000410	AU 1999-60392	19990913
EP 1115887	A1	20010718	EP 1999-969450	19990913
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002526511	T2	20020820	JP 2000-574297	19990913
US 2003099945	A1	20030529	US 2001-916443	20010730

PRIORITY APPLN. INFO.: US 1994-309245 A2 19940920
US 1996-618700 A2 19960320
US 1990-536428 B2 19900611

Search completed by David Schreiber 308-4292

US 1991-714131 A2 19910610
US 1998-157601 A 19980921
WO 1999-US21079 W 19990913
US 2000-546657 B1 20000410

AB This invention discloses a method for parallel SELEX (Systematic **Evolution** of Ligands by Exponential enrichment), consisting of prepg. a nucleic acid test mixt., coupling each nucleic acid to a small org. mol., forming a product library via bond formation of the attached org. mols. with free reactant(s) **catalyzed** by their attached nucleic acids, and selecting desired products, both for identification and for amplification of their **catalytic** nucleic acids. In this process, a large nucleic acid test mixt. is provided with each nucleic acid linked to a chem. reactant, premised on the assumption that in the library there will be nucleic acids capable of mediating a reaction between their own attached reactants and some other free reactants. Sepg. the desired products, then, allows for enrichment of their attached **catalytic** nucleic acids. Parallel SELEX can include the formation of product libraries using asym. reactions. Unlike conventional **combinatorial** chem. approaches, the reactions can be included with no knowledge of the stereochem. outcome. Generic examples using the parallel SELEX method are given.

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 31 OF 56 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 2000:242399 SCISEARCH
THE GENUINE ARTICLE: 296KL
TITLE: Kinetic framework for ligation by an efficient RNA ligase ribozyme
AUTHOR: Bergman N H; Johnston W K; Bartel D P (Reprint)
CORPORATE SOURCE: MIT, WHITEHEAD INST BIOMED RES, CAMBRIDGE CTR 9, CAMBRIDGE, MA 02142 (Reprint); MIT, WHITEHEAD INST BIOMED RES, CAMBRIDGE CTR 9, CAMBRIDGE, MA 02142; MIT, DEPT BIOL, CAMBRIDGE CTR 9, CAMBRIDGE, MA 02142
COUNTRY OF AUTHOR: USA
SOURCE: BIOCHEMISTRY, (21 MAR 2000) Vol. 39, No. 11, pp. 3115-3123

Publisher: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036.
ISSN: 0006-2960.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 37

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The class I RNA ligase ribozyme, isolated previously from **random** sequences, performs an efficient RNA ligation reaction. It ligates two substrate RNAs, promoting the attack of the 3'-hydroxyl of one substrate upon the 5'-triphosphate of the other substrate with release of pyrophosphate. This ligation reaction has similarities to the reaction **catalyzed** by RNA polymerases. Using data from steady-state kinetic measurements and pulse-chase/pH-jump experiments, we have constructed minimal kinetic frameworks for two versions of the class I ligase, named 207t and 210t. For both ligases, as well as for the self-ligating parent ribozyme, the rate constant for the chemical step (k(c)) is log-linear with pH in the range 5.7-8.0. At physiological pH, the k(c) is 100 min(-1), a value similar to these reported for the fastest naturally occurring ribozymes. At higher pH, product release is limiting for both 207t and 210t. The 210t ribozyme, with its faster product release, attains

multiple-turnover rates (k(cat) = 360 min(-1), pH 9.0) exceeding those of 207t and other reported ribozyme reactions. The kinetic framework for the 210t ribozyme describes the limits of this **catalysis** and suggests how key steps can be targeted for improvement using design or **combinatorial** approaches.

L22 ANSWER 32 OF 56 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 2000124000 MEDLINE
DOCUMENT NUMBER: 20124000 PubMed ID: 10656819
TITLE: Display of active subtilisin 309 on phage: analysis of parameters influencing the selection of subtilisin variants with changed substrate specificity from libraries using phosphonylating inhibitors.
AUTHOR: Legendre D; Laraki N; Graslund T; Bjornvad M E; Bouchet M; Nygren P A; Borchert T V; Fastrez J
CORPORATE SOURCE: Laboratoire de Biochimie Physique et des biopolymeres, Universite catholique de Louvain, Place L. Pasteur, 1-1b, Louvain-la-Neuve, 1348, Belgium.
SOURCE: JOURNAL OF MOLECULAR BIOLOGY, (2000 Feb 11) 296 (1) 87-102. Journal code: 2985088R. ISSN: 0022-2836.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000327
Last Updated on STN: 20000327
Entered Medline: 20000314

AB Many attempts have been made to endow enzymes with new **catalytic** activities. One general strategy involves the creation of **random combinatorial** libraries of mutants associated with an efficient screening or selection scheme. Phage display has been shown to greatly facilitate the selection of polypeptides with desired properties by establishing a close link between the polypeptide and the gene that encodes it. Selection of phage displayed enzymes for new **catalytic** activities remains a challenge. The aim of this study was to display the serine protease subtilisin 309 (savinase) from Bacillus lentus on the surface of filamentous fd phage and to develop selection schemes that allow the extraction of subtilisin variants with a changed substrate specificity from libraries. Subtilisins are produced as secreted preproenzyme that mature in active enzyme autocatalytically. They have a broad substrate specificity but exhibit a significant preference for hydrophobic residues and very limited reactivity toward charged residues at the P4 site in the substrate. Here, we show that savinase can be functionally displayed on phage in the presence of the proteic inhibitor CI2. The free enzyme is released from its complex with CI2 upon addition of the anionic detergent LAS. The phage-enzyme can be panned on streptavidin beads after labelling by reaction with (biotin-N-epsilon-aminocaproyl-cystamine-N'-glutaryl)-l-Ala-l-Ala-l-Pro-Phe(P)-diphenyl ester. Reactions of libraries, in which residues 104 and 107 forming part of the S4 pocket have been randomised, with (biotin-N-epsilon-aminocaproyl-cystamine-N'-glutaryl)-alpha-l-Lys-l-Ala-l-Pro-Phe(P)-diphenylester allowed us to select enzymes with increased specific activity for a substrate containing a lysine in P4. Parameters influencing the selection as for instance the efficiency of maturation of mutant enzymes in libraries have been investigated.
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L22 ANSWER 33 OF 56 HCAPLUS COPYRIGHT 2003 ACS on STN

Search completed by David Schreiber 308-4292

Zhou 09/909,038

ACCESSION NUMBER: 1999:45047 HCAPLUS
DOCUMENT NUMBER: 130:91264
TITLE: Parallel SELEX allowing for asymmetrical reactions in **combinatorial** chemistry
INVENTOR(S): Eaton, Bruce; Gold, Larry
PATENT ASSIGNEE(S): Nexstar Pharmaceuticals, Inc., USA
SOURCE: U.S., 51 pp., Cont.-in-part of U.S. 5,723,289.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 121
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5858660	A	19990112	US 1996-618700	19960320
US 5723289	A	19980303	US 1994-309245	19940920
US 6048698	A	20000411	US 1998-157601	19980921
US 2003099945	A1	20030529	US 2001-916443	20010730

PRIORITY APPLN. INFO.:

US 1994-309245	A2	19940920
US 1990-536428	B2	19900611
US 1991-714131	A2	19910610
US 1996-618700	A2	19960320
US 1998-157601	A1	19980921
US 2000-546657	B1	20000410

AB This invention discloses a method for parallel SELEX (Systematic **Evolution** of Ligands by Exponential enrichment), consisting of prepg. a nucleic acid test mixt., coupling each nucleic acid to a small org. mol., forming a product library via bond formation of the attached org. mols. with free reactant(s) **catalyzed** by their attached nucleic acids, and selecting desired products, both for identification and for amplification of their **catalytic** nucleic acids. In this process, a large nucleic acid test mixt. is provided with each nucleic acid linked to a chem. reactant, premised on the assumption that in the library there will be nucleic acids capable of mediating a reaction between their own attached reactants and some other free reactants. Sepg. the desired products, then, allows for enrichment of their attached **catalytic** nucleic acids. Parallel SELEX can include the formation of product libraries using asym. reactions. Unlike conventional **combinatorial** chem. approaches, the reactions can be included with no knowledge of the stereochem. outcome. Generic examples using the parallel SELEX method are given.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 34 OF 56 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 1999:703693 SCISEARCH
THE GENUINE ARTICLE: 234MK
TITLE: Dynamic **combinatorial** chemistry and virtual **combinatorial** libraries
AUTHOR: Lehn J M (Reprint)
CORPORATE SOURCE: UNIV STRASBOURG 1, LAB CHEM SUPRAMOL, 4 RUE BLASE PASCAL, F-67000 STRASBOURG, FRANCE (Reprint)
COUNTRY OF AUTHOR: FRANCE
SOURCE: CHEMISTRY-A EUROPEAN JOURNAL, (SEP 1999) Vol. 5, No. 9, pp. 2455-2463.
Publisher: WILEY-V C H VERLAG GMBH, MUHLENSTRASSE 33-34, D-13187 BERLIN, GERMANY.
ISSN: 0947-6539.

Search completed by David Schreiber 308-4292

Zhou 09/909,038

DOCUMENT TYPE: Article; Journal
FILE SEGMENT: PHYS
LANGUAGE: English
REFERENCE COUNT: 70

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Whereas **combinatorial** chemistry is based on extensive libraries of prefabricated molecules, dynamic **combinatorial** chemistry (DCC) implements the reversible connection of sets of basic components to give access to virtual **combinatorial** libraries (VCLs), whose constituents comprise all possible combinations that may potentially be generated. The constituent(s) actually expressed among all those accessible is(are) expected to be that(those) presenting the strongest interaction with the target, that is, the highest receptor/substrate molecular recognition. The overall process is thus instructed (target-driven), **combinatorial**, and dynamic. It bypasses the need to actually synthesize the constituents of a **combinatorial** library by letting the target perform the assembly of the optimal partner. It comprizes both molecular and supramolecular events. The basic features of the DCC/VCL approach are presented together with its implementation in different fields and the perspectives it offers in a variety of areas of science and technology, such as the discovery of biologically active substances, of novel materials, of efficient **catalysts**, and so forth. Finally, it participates in the progressive development of an adaptive chemistry.

L22 ANSWER 35 OF 56 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1999:526839 BIOSIS
DOCUMENT NUMBER: PREV199900526839
TITLE: A high-throughput digital imaging screen for the discovery and directed **evolution** of oxygenases.
AUTHOR(S): Joo, Hyun; Arisawa, Akira; Lin, Zhanglin; Arnold, Frances H. (1)
CORPORATE SOURCE: (1) Division of Chemistry and Chemical Engineering 210-41, California Institute of Technology, Pasadena, CA, 91125 USA
SOURCE: Chemistry & Biology (London), (Oct., 1999) Vol. 6, No. 10, pp. 699-706.
ISSN: 1074-5521.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Background: Oxygenases **catalyze** the hydroxylation of a wide variety of organic substrates. An ability to alter oxygenase substrate specificities and improve their activities and stabilities using **recombinant** DNA techniques would expand their use in processes such as chemical synthesis and bioremediation. Discovery and directed **evolution** of oxygenases require efficient screens that are sensitive to the activities of interest and can be applied to large numbers of crude enzyme samples. Results: Horseradish peroxidase (HRP) couples the phenolic products of hydroxylation of aromatic substrates to generate colored and/or fluorescent compounds that are easily detected spectroscopically in high-throughput screening. Coexpression of the coupling enzyme with a functional mono- or dioxygenase creates a pathway for the conversion of aromatic substrates into fluorescent compounds in vivo. We used this approach for detecting the products of the toluene-dioxygenase-**catalyzed** hydroxylation of chlorobenzene and to screen large mutant libraries of Pseudomonas putida cytochrome P450cam by fluorescence digital imaging. Colors generated by the HRP coupling reaction are sensitive to the site of oxygenase-**catalyzed** hydroxylation, allowing the screen to be used to identify

Search completed by David Schreiber 308-4292

catalysts with new or altered regiospecificities. Conclusions: The coupled oxygenase-peroxidase reaction system is well suited for screening oxygenase libraries to identify mutants with desired features, including higher activity or stability and altered reaction specificity. This approach should also be useful for screening expressed DNA libraries and **combinatorial** chemical libraries for hydroxylation **catalysts** and for optimizing oxygenase reaction conditions.

L22 ANSWER 36 OF 56 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 1999:733755 SCISEARCH
THE GENUINE ARTICLE: 238CK
TITLE: In vitro selection of functional nucleic acids
AUTHOR: Wilson D S (Reprint); Szostak J W
CORPORATE SOURCE: MASSACHUSETTS GEN HOSP, HOWARD HUGHES MED INST, BOSTON, MA 02114 (Reprint); MASSACHUSETTS GEN HOSP, DEPT MOL BIOL, BOSTON, MA 02114
COUNTRY OF AUTHOR: USA
SOURCE: ANNUAL REVIEW OF BIOCHEMISTRY, (SEP 1999) Vol. 68, pp. 611-647.
Publisher: ANNUAL REVIEWS INC, 4139 EL CAMINO WAY, PO BOX 10139, PALO ALTO, CA 94303-0139.
ISSN: 0066-4154.
DOCUMENT TYPE: General Review; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 203
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB In vitro selection allows rare functional RNA or DNA molecules to be isolated from pools of over 10(15) different sequences. This approach has been used to identify RNA and DNA ligands for numerous small molecules, and recent three-dimensional **structure** solutions have revealed the basis for ligand recognition in several cases. By selecting high-affinity and -specificity nucleic acid ligands for proteins, promising new therapeutic and diagnostic reagents have been identified. Selection experiments have also been carried out to identify ribozymes that **catalyze** a variety of chemical transformations, including RNA cleavage, ligation, and synthesis, as well as alkylation and acyl-transfer reactions and N-glycosidic and peptide bond formation. The existence of such RNA enzymes supports the notion that ribozymes could have directed a primitive metabolism before the **evolution** of protein synthesis. New in vitro protein selection techniques should allow for a direct comparison of the frequency of ligand binding and **catalytic structures** in pools of **random** sequence polynucleotides versus polypeptides.

L22 ANSWER 37 OF 56 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 1999305106 EMBASE
TITLE: A statistical chemistry approach to the origin of life.
AUTHOR: Segre D.; Lancet D.
CORPORATE SOURCE: D. Lancet, Molec. Genetics/Genome Center Dept., Weizmann Institute of Science, Rehovot 76100, Israel
SOURCE: Chemtracts, (1999) 12/6 (382-397).
Refs: 81
ISSN: 1431-9268 CODEN: CHEMFW
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 021 Developmental Biology and Teratology
022 Human Genetics

Search completed by David Schreiber 308-4292

Zhou 09/909,038

LANGUAGE: English
SUMMARY LANGUAGE: English
AB We revisit some theoretical models dealing with the chemical emergence of lifelike properties in prebiotic systems. Special emphasis is given to models involving **random** assemblies of mutually **catalytic** organic molecules, as opposed to scenarios in which individual molecular species are endowed with the capacity of self-replication. We highlight here the challenge of tracing the very first steps of biogenesis, when self-replication, **mutation**, selection, and **evolution** may have been hardly recognizable. The models we discuss share the assumption that a large repertoire of relatively simple organic compounds could spontaneously form prebiotically, and the notion that a statistical approach, independent of detailed molecular properties, can uncover some general principles underlying biogenic processes. Fundamental models, put forward by Dyson and Kauffman, describe very early scenarios, whose statistical nature is reflected in the possibility of characterizing many **random**, mutually **catalytic** interactions with relatively few parameters. Further theoretical considerations indicate that mutually **catalytic** assemblies might also entail a primitive information transfer system, exclusively based on idiosyncratic chemical **compositions**, a situation described here as the inheritance of a ' **compositional** genome.' Amphiphilic molecules, due to their peculiar attributes, are suggested to potentially embody many of the properties necessary for these systems to emerge spontaneously, hinting to the possibility of an exclusively lipid-based origin of life. We stress that modem trends in molecular complementarity, **combinatorial** chemistry, and enzyme mimetics represent a source of conceptual and experimental information that can help extend previous models. This is exemplified here by the Graded Autocatalysis Replication Domain (GARD) model we developed, based on a statistical distribution of **catalytic** activities. A further extension of this model, the Amphiphile-GARD, aims at a more realistic and testable theoretical description of some scenarios for early prebiotic **evolution**.

L22 ANSWER 38 OF 56 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 1999:439256 SCISEARCH
THE GENUINE ARTICLE: 202UG
TITLE: Host-guest chemistry: **combinatorial** receptors
AUTHOR: Linton B (Reprint); Hamilton A D
CORPORATE SOURCE: YALE UNIV, STERLING CHEM LAB, BOX 208107, NEW HAVEN, CT 06520 (Reprint)
COUNTRY OF AUTHOR: USA
SOURCE: CURRENT OPINION IN CHEMICAL BIOLOGY, (JUN 1999) Vol. 3, No. 3, pp. 307-312.
Publisher: CURRENT BIOLOGY LTD, 34-42 CLEVELAND STREET, LONDON W1P 6LE, ENGLAND.
ISSN: 1367-5931.
DOCUMENT TYPE: General Review; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 30
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB A **combinatorial** approach to receptor design provides an expedient method to discover the most effective host-guest complexes from within a library. Recent advances focus on **generation** of larger libraries, facile detection, **combinatorial catalysis** and the formation of dynamic receptor libraries.

L22 ANSWER 39 OF 56 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN

Search completed by David Schreiber 308-4292

Zhou 09/909,038

ACCESSION NUMBER: 1999:48334 SCISEARCH
THE GENUINE ARTICLE: BM15C
TITLE: Superior biocatalysts by directed **evolution**
AUTHOR: Reetz M T (Reprint); Jaeger K E
CORPORATE SOURCE: MAX PLANCK INST KOHLENFORSCH, D-45470 MULHEIM, GERMANY (Reprint); RUHR UNIV, LEHRSTUHL BIOL MIKROORGANISMEN, D-44780 BOCHUM, GERMANY
COUNTRY OF AUTHOR: GERMANY
SOURCE: TOPICS IN CURRENT CHEMISTRY, (OCT 1999) Vol. 200, pp. 31-57.
Publisher: SPRINGER-VERLAG BERLIN, HEIDELBERGER PLATZ 3, W-1000 BERLIN 33, GERMANY.
ISSN: 0342-6793.
DOCUMENT TYPE: General Review; Journal
FILE SEGMENT: PHYS
LANGUAGE: English
REFERENCE COUNT: 134
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Useful biocatalysts for organic chemistry can be created by directed **evolution**. **Mutations** are introduced into genes encoding biocatalyst proteins of interest by error-prone PCR or other **random** mutagenesis methods. The **mutated** genes can be rearranged by **recombinative** processes like DNA shuffling, thereby significantly enhancing the efficiency with which genes can be evolved. These genes are expressed in suitable microbial hosts leading to the production of functional biocatalysts. Selection or screening procedures serve to identify in a large library of potential candidates the biocatalyst which possesses the desired properties. Examples of applications include subtilisin E with greatly improved **catalytic** activity and stability in organic solvent, an esterase with 50-fold higher activity in organic solvent, and a beta-lactamase conferring a 32,000-fold increased antibiotic resistance. Furthermore, directed **evolution** of a bacterial lipase resulted in a significant increase in enantioselectivity, thereby demonstrating the enormous potential of this process for organic chemistry.

L22 ANSWER 40 OF 56 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 1999180409 MEDLINE
DOCUMENT NUMBER: 99180409 PubMed ID: 10082372
TITLE: Probing enzyme quaternary **structure** by **combinatorial** mutagenesis and selection.
AUTHOR: MacBeath G; Kast P; Hilvert D
CORPORATE SOURCE: Department of Chemistry, The Scripps Research Institute, La Jolla, California 92037, USA.
SOURCE: PROTEIN SCIENCE, (1998 Aug) 7 (8) 1757-67.
Journal code: 9211750. ISSN: 0961-8368.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199905
ENTRY DATE: Entered STN: 19990601
Last Updated on STN: 19990601
Entered Medline: 19990519

AB Genetic selection provides an effective way to obtain active **catalysts** from a diverse population of protein variants. We have used this tool to investigate the role of loop sequences in determining the quaternary **structure** of a domain-swapped enzyme. By inserting **random** loops of four to seven residues into a dimeric

Search completed by David Schreiber 308-4292

chorismate mutase and selecting for functional variants by genetic complementation, we have obtained and characterized both monomeric and hexameric enzymes that retain considerable **catalytic** activity. The low percentage of active proteins recovered from these selection experiments indicates that relatively few loop sequences permit a change in quaternary **structure** without affecting active site **structure**. The results of our experiments suggest further that protein stability can be an important driving force in the **evolution** of oligomeric proteins.

L22 ANSWER 41 OF 56 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 1998:553154 SCISEARCH
THE GENUINE ARTICLE: ZZ732
TITLE: Determination of the amino acid requirements for a protein hinge in triosephosphate isomerase
AUTHOR: Sun S H; Sampson N S (Reprint)
CORPORATE SOURCE: SUNY STONY BROOK, DEPT CHEM, STONY BROOK, NY 11794 (Reprint); SUNY STONY BROOK, DEPT CHEM, STONY BROOK, NY 11794
COUNTRY OF AUTHOR: USA
SOURCE: PROTEIN SCIENCE, (JUL 1998) Vol. 7, No. 7, pp. 1495-1505. Publisher: CAMBRIDGE UNIV PRESS, 40 WEST 20TH STREET, NEW YORK, NY 10011-4211. ISSN: 0961-8368.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 40
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We have determined the sequence requirements for a protein hinge in triosephosphate isomerase. The codons encoding the hinge at the C-terminus of the active-site lid of triosephosphate isomerase were replaced with a genetic library of all possible 8,000 amino acid **combinations**. The most active of these 8,000 mutants were selected using in vivo complementation of a triosephosphate isomerase deficient strain of E. coli, DF502. Approximately 3% of the mutants complement DF502 with an activity that is above 70% of wild-type activity. The sequences of these hinge mutants reveal that the solutions to the hinge flexibility problem an varied. Moreover, these preferences are sequence dependent; that is, certain pairs occur frequently. They fall into six families of similar sequences. In addition to the hinge sequences expected on the basis of phylogenetic analysis, we selected three new families of 3-amino-acid hinges: X(A/S)(L/K/M), X(aromatic/beta-branched)(L/K), and XP(S/N). The absence of these hinge families in the more than 60 known species of triosephosphate isomerase suggests that during **evolution**, not all of sequence space is sampled, perhaps because there is no neutral **mutation** pathway to access the other families.

L22 ANSWER 42 OF 56 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 1998408204 MEDLINE
DOCUMENT NUMBER: 98408204 PubMed ID: 9735271
TITLE: A **stochastic** model for the rapid emergence of specific vertebrate immunity incorporating horizontal transfer of systems enabling duplication and **combinational** diversification.
AUTHOR: Marchalonis J J; Schluter S F
CORPORATE SOURCE: Department of Microbiology and Immunology, University of Arizona, Tucson 85724-5049, USA.
SOURCE: JOURNAL OF THEORETICAL BIOLOGY, (1998 Aug 7) 193 (3)

Search completed by David Schreiber 308-4292

429-44.
Journal code: 0376342. ISSN: 0022-5193.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199810
ENTRY DATE: Entered STN: 19981029
Last Updated on STN: 19981029
Entered Medline: 19981016

AB Recent molecular data indicate that the antigen-specific **combinatorial** immune response is restricted to jawed vertebrates where it is found in representatives of all class from cartilagenous fishes to mammals. Here, we analyse the relatively rapid emergence of the **combinatorial** system terms of three **stochastic** process, with the system reaching essentially full capacity in immunoglobulin recognition elements and diversification and **recombination** of gene segments in an **evolutionary** span of time of less than 20 million years. The mechanisms for inducibility were coopted from ancient and widely spread processes in phylogeny for regulation of cell division. The proposed process of formation entailed the **evolution** of unknown ancestral genes into those specifying bona fide immunoglobulin domains, and the **generation** of multiple copies of these via a series of events facilitated by horizontal transfer of site-specific **recombinases** and **recombination** signal sequences most probably from microbial and fungal sources. The second process is one of rapid "decay" (**evolution**) which occurred in about 10 million year under stringent selective conditions to generate proper conserved canonical sequences. The third process is that of the long term **evolution** of these characteristic immunoglobulin domains over the 450 million years since their emergence. As a first approximation the rates of these three processes were computed using first order differential equations. The rate of formation has a magnitude of 10-7 substitutions per site per year, and that of rapid modifications is 10-8 substitutions per site per year. The long term rate of immunoglobulin **evolution** is comparable to that of other moderately conserved proteins, (1-3) x 10-9 substitutions per site per year). This model is testable by searching for "footprints" of microbial and fungal DNA processing enzymes and **recombination** mechanisms. The hypothesis raises the general concept that horizontal transfer of genes facilitating rearrangement and duplication can **catalyse** major steps of macroevolution.

L22 ANSWER 43 OF 56 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 97:720302 SCISEARCH
THE GENUINE ARTICLE: XX399
TITLE: Phage display of a **catalytic** antibody to optimize affinity for transition-state analog binding
AUTHOR: Baca M; Scanlan T S; Stephenson R C; Wells J A (Reprint)
CORPORATE SOURCE: GENENTECH INC, DEPT PROT ENGN, 460 POINT SAN BRUNO BLVD, S SAN FRANCISCO, CA 94080 (Reprint); GENENTECH INC, DEPT PROT ENGN, S SAN FRANCISCO, CA 94080; UNIV CALIF SAN FRANCISCO, DEPT PHARMACEUT CHEM, SAN FRANCISCO, CA 94143
COUNTRY OF AUTHOR: USA
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (16 SEP 1997) Vol. 94, No. 19, pp. 10063-10068.
Publisher: NATL ACAD SCIENCES, 2101 CONSTITUTION AVE NW, WASHINGTON, DC 20418.

Search completed by David Schreiber 308-4292

ISSN: 0027-8424.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 33

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB **Catalytic** antibodies have shown great promise for **catalyzing** a tremendously diverse set of natural and unnatural chemical transformations. However, few **catalytic** antibodies have efficiencies that approach those of natural enzymes, In principle, **random** mutagenesis procedures such as phage display could be used to improve the **catalytic** activities of existing antibodies; however, these studies have been hampered by difficulties in the **recombinant** expression of antibodies, Here, we have grafted the antigen binding loops from a murine-derived **catalytic** antibody, 17E8, onto a human antibody framework in an effort to overcome difficulties associated with **recombinant** expression and phage display of this antibody, ''Humanized'' 17E8 retained similar **catalytic** and hapten binding properties as the murine antibody while levels of functional Fab displayed on phage were 200-fold higher than for a murine variable region/human constant region chimeric Fab, This construct was used to prepare **combinatorial** libraries. Affinity panning of these resulted in the selection of variants with 2- to 8-fold improvements in binding affinity for a phosphonate transition-state analog, Surprisingly, none of the affinity-matured variants was more **catalytically** active than the parent antibody and some were significantly less active, By contrast, a weaker binding variant was identified with 2-fold greater **catalytic** activity and incorporation of a single substitution (Tyr-100a(H)-->Asn) from this variant into the parent antibody led to a 5-fold increase in **catalytic** efficiency, Thus, phage display methods can be readily used to optimize binding of **catalytic** antibodies to transition-state analogs, and when used in conjunction with limited screening for **catalysis** can identify variants with higher **catalytic** efficiencies.

L22 ANSWER 44 OF 56 MEDLINE on STN

ACCESSION NUMBER: 97365677 MEDLINE
DOCUMENT NUMBER: 97365677 PubMed ID: 9222504
TITLE: Interacting RNA species identified by **combinatorial** selection.
AUTHOR: Cho B; Taylor D C; Nicholas H B Jr; Schmidt F J
CORPORATE SOURCE: Department of Biochemistry, University of Missouri-Columbia 65212, USA.
CONTRACT NUMBER: LM05513 (NLM)
SOURCE: BIOORGANIC AND MEDICINAL CHEMISTRY, (1997 Jun) 5 (6) 1107-13.
Journal code: 9413298. ISSN: 0968-0896.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U34759
ENTRY MONTH: 199708
ENTRY DATE: Entered STN: 19970908
Last Updated on STN: 19970908
Entered Medline: 19970826

AB RNA molecules were selected from a **random** sequence library for their ability to bind to an RNA stem-loop target. Oligonucleotides with

extensive Watson-Crick complementarity to the RNA ligand were selected against by inclusion of a blocking oligodeoxynucleotide in the binding phase of the selection protocol. After 18 **generations** of SELEX (systematic **evolution** of ligands by exponential enrichment) a single RNA family was predominant in the binding population. The winning aptamer RNA bound the target RNA with an apparent Kd = 70 nM. **Structural** mapping and Fe(II)-EDTA protection indicated that the target RNA interacted with small unpaired loops in the aptamer **structure**.

L22 ANSWER 45 OF 56 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:745572 HCAPLUS
DOCUMENT NUMBER: 128:85520
TITLE: Accessing rare activities from **random** RNA sequences: the importance of the length of molecules in the starting pool
AUTHOR(S): Sabeti, Pardis C.; Unrau, Peter J.; Bartel, David P.
CORPORATE SOURCE: Department of Biology, Whitehead Institute for Biomedical Research, Massachusetts Institute of Technology, Cambridge, MA, 02142, USA
SOURCE: Chemistry & Biology (1997), 4(10), 767-774
CODEN: CBOLE2; ISSN: 1074-5521
PUBLISHER: Current Biology Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In the past few years, numerous binding and **catalytic** motifs have been isolated from pools of **random** nucleic acid sequences. To extend the utility of this approach, it is important to learn how to design **random**-sequence pools that provide maximal access to rare activities. In an effort to better define the relative merits of longer and shorter pools (i.e. pools with longer or shorter **random** -sequence segments), we have examd. the inhibitory effect of excess arbitrary sequence on ribozyme activity and have evaluated whether this inhibition overshadows the calcd. advantage of longer pools. The calcd. advantage of longer sequences was highly dependent on the size and complexity of the desired motif. Small, simple motifs were not much more abundant in longer mols. In contrast, larger motifs, particularly the most complex (highly modular) motifs, were much more likely to be present in longer mols. The exptl. detd. inhibition of activity by excess sequence was moderate, with bulk effects among four libraries ranging from no effect to 18-fold inhibition. The median effect among 60 clones was fivefold inhibition. In conclusion, for accessing simple motifs (e.g. motifs at least as small and simple as the hammerhead ribozyme motif), longer pools have little if any advantage. For more complex motifs, the inhibitory effect of excess sequence does not approach the calcd. advantage of pools of longer mols. Thus, when seeking to access rare activities, the length of typical **random**-sequence pools (.ltoreq.70 **random** positions) is shorter than optimal. As this conclusion holds over a range of incubation conditions, it may also be relevant when considering the emergence of new functional motifs during early **evolution**.
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 46 OF 56 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 1998:3661 SCISEARCH
THE GENUINE ARTICLE: YL037
TITLE: Directed **evolution** of enzyme **catalysts**
AUTHOR: Kuchner O (Reprint); Arnold F H

Search completed by David Schreiber 308-4292

Zhou 09/909,038

CORPORATE SOURCE: CALTECH, DIV CHEM & CHEM ENGN 210 41, PASADENA, CA 91125 (Reprint)
COUNTRY OF AUTHOR: USA
SOURCE: TRENDS IN BIOTECHNOLOGY, (DEC 1997) Vol. 15, No. 12, pp. 523-530.
Publisher: ELSEVIER SCI LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD, OXON, ENGLAND OX5 1GB.
ISSN: 0167-7799.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; AGRI
LANGUAGE: English
REFERENCE COUNT: 51
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Directed enzyme **evolution** has emerged in the past few years as a powerful alternative to rational approaches for engineering biocatalysts. Prerequisites for successful directed **evolution** are functional expression in a suitable microbial host, a rapid screen for the desired feature(s) and a well-thought-out working strategy for navigating protein landscapes. The rapidly growing body of literature on enzyme **evolution** in vitro includes techniques for creating and searching **combinatorial** enzyme libraries, as well as several successful examples of different **evolutionary** strategies being used.

L22 ANSWER 47 OF 56 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:235215 HCAPLUS
DOCUMENT NUMBER: 128:235608
TITLE: Accelerated syntheses and screening of stereoselective transition metal **catalysts**
AUTHOR(S): Burgess, Kevin; Porte, Alex M.
CORPORATE SOURCE: Department of Chemistry, Texas AandM University, College Station, TX, USA
SOURCE: Advances in Catalytic Processes (1997), 2(Asymmetric Catalysis), 69-82
CODEN: ACPRFB
PUBLISHER: JAI Press Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 58 refs. on topics of: parallel in the biotechnol. and pharmaceutical industries, **evolution** of methods for **generation** and screening of transition metal **catalyst** libraries, libraries of transition metal complexes: demonstration of high throughput screening, easily constructed ligands, divergent ligand syntheses, solid phrase syntheses of ligands.

REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 48 OF 56 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 97:380589 SCISEARCH
THE GENUINE ARTICLE: WY279
TITLE: In vivo versus in vitro screening or selection for **catalytic** activity in enzymes and abzymes
AUTHOR: Fastrez J
CORPORATE SOURCE: LAB BIOCHIM PHYS & BIOPOLYMERES, B-1348 LOUVAIN, BELGIUM
COUNTRY OF AUTHOR: BELGIUM
SOURCE: MOLECULAR BIOTECHNOLOGY, (FEB 1997) Vol. 7, No. 1, pp. 37-55.
Publisher: HUMANA PRESS INC, 999 RIVERVIEW DRIVE SUITE 208, TOTOWA, NJ 07512.

Search completed by David Schreiber 308-4292

ISSN: 1073-6085.
DOCUMENT TYPE: General Review; Journal
LANGUAGE: English
REFERENCE COUNT: 145

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The recent development of **catalytic** antibodies and the introduction of new techniques to generate huge libraries Of **random** mutants Of existing enzymes have created the need for powerful tools for finding in large populations of cells those producing the **catalytically** most active proteins. Several approaches have been developed and used to reach this goal. The screening techniques aim at easily detecting the clones producing active enzymes or abzymes; the selection techniques are designed to extract these clones from mixtures: These techniques have been applied both in vivo and in vitro. This review describes the advantages and limitations Of the various methods in terms of ease of use, sensitivity, and convenience for handling large libraries. Examples are analyzed and tentative rules proposed. These techniques prove to be quite powerful to study the relationship between **structure** and function and to alter the properties of enzymes.

L22 ANSWER 49 OF 56 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 96:416187 SCISEARCH
THE GENUINE ARTICLE: UN253
TITLE: ACTIVE BARNASE VARIANTS WITH COMPLETELY **RANDOM** HYDROPHOBIC CORES
AUTHOR: AXE D D (Reprint); FOSTER N W; FERSHT A R
CORPORATE SOURCE: UNIV CAMBRIDGE, DEPT CHEM, MRC, UNIT PROT FUNCT & DESIGN, LENSFIELD RD, CAMBRIDGE CB2 1EW, ENGLAND (Reprint)
COUNTRY OF AUTHOR: ENGLAND
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (28 MAY 1996) Vol. 93, No. 11, pp. 5590-5594.
ISSN: 0027-8424.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 33

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The central **structural** feature of natural proteins is a tightly packed and highly ordered hydrophobic core. If some measure of exquisite, native-like core packing is necessary for enzymatic function, this would constitute a significant obstacle to the development of novel enzymes, either by design or by natural or experimental **evolution** . To test the minimum requirements for a core to provide sufficient **structural** integrity for enzymatic activity, we have produced mutants of the ribonuclease barnase in which 12 of the 13 core residues have together been randomly replaced by hydrophobic alternatives. Using a sensitive biological screen, we find that a strikingly high proportion of these mutants (23%) retain enzymatic activity in vivo. Further substitution at the 13th core position shows that a similar proportion of completely **random** hydrophobic cores supports enzyme function. Of the active mutants produced, several have no wild-type core residues. These results imply that hydrophobicity is nearly a sufficient criterion for the construction of a functional core and, in conjunction with previous studies, that refinement of a crudely functional core entails more stringent sequence constraints than does the initial attainment of crude core function. Since attainment of crude function is the critical initial step in **evolutionary** innovation, the relatively scant requirements contributed by the hydrophobic core would greatly reduce the

initial hurdle on the **evolutionary** pathway to novel enzymes. Similarly, experimental development of novel functional proteins might be simplified by limiting core design to mere specification of hydrophobicity and using iterative **mutation**-selection to optimize core **structure.**

L22 ANSWER 50 OF 56 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 96:868304 SCISEARCH
THE GENUINE ARTICLE: VT621
TITLE: Genetic selection strategies for generating and characterizing **catalysts**
AUTHOR: Kast P (Reprint); Hilvert D
CORPORATE SOURCE: SCRIPPS CLIN & RES FDN, DEPT CHEM, 10666 N TORREY PINES RD, LA JOLLA, CA 92037 (Reprint); SCRIPPS CLIN & RES FDN, DEPT MOL BIOL, LA JOLLA, CA 92037
COUNTRY OF AUTHOR: USA
SOURCE: PURE AND APPLIED CHEMISTRY, (NOV 1996) Vol. 68, No. 11, pp. 2017-2024.
Publisher: BLACKWELL SCIENCE LTD, OSNEY MEAD, OXFORD, OXON, ENGLAND OX2 0EL.
ISSN: 0033-4545.
DOCUMENT TYPE: General Review; Journal
FILE SEGMENT: PHYS
LANGUAGE: English
REFERENCE COUNT: 102
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Molecular **evolution** is a powerful tool for exploring and creating **catalytic** function in biological macromolecules. This review focuses on examples and current strategies for the application of **random** mutagenesis of target genes coupled with direct selection in vivo. The technology is illustrated by the dissection of **catalytic** features in chorismate mutase. Future avenues for identifying and evolving **catalytic** antibodies are also discussed.

L22 ANSWER 51 OF 56 MEDLINE on STN
ACCESSION NUMBER: 2001657987 MEDLINE
DOCUMENT NUMBER: 97617893 PubMed ID: 11539421
TITLE: Chance and necessity in the selection of nucleic acid **catalysts.**
AUTHOR: Lorsch J R; Szostak J W
CORPORATE SOURCE: Department of Molecular Biology, Massachusetts General Hospital, Boston 02114, USA.
SOURCE: Acc Chem Res, (1996 Feb) 29 (2) 103-10. Ref: 57
Journal code: 0157313. ISSN: 0001-4842.
(Investigators: Szostak J W, MA Gen Hosp, Boston) Report No.: NASA-00020560.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Space Life Sciences
ENTRY MONTH: 199707
ENTRY DATE: Entered STN: 20011119
Last Updated on STN: 20011119
Entered Medline: 19970726

AB In Tom Stoppard's famous play [Rosencrantz and Guildenstern are Dead], the ill-fated heroes toss a coin 101 times. The first 100 times they do so

the coin lands heads up. The chance of this happening is approximately 1 in 10(30), a sequence of events so rare that one might argue that it could only happen in such a delightful fiction. Similarly rare events, however, may underlie the origins of biological **catalysis**. What is the probability that an RNA, DNA, or protein molecule of a given **random** sequence will display a particular **catalytic** activity? The answer to this question determines whether a collection of such sequences, such as might result from prebiotic chemistry on the early earth, is extremely likely or unlikely to contain **catalytically** active molecules, and hence whether the origin of life itself is a virtually inevitable consequence of chemical laws or merely a bizarre fluke. The fact that a priori estimates of this probability, given by otherwise informed chemists and biologists, ranged from 10(-5) to 10(-50), inspired us to begin to address the question experimentally. As it turns out, the chance that a given **random** sequence RNA molecule will be able to **catalyze** an RNA polymerase-like phosphoryl transfer reaction is close to 1 in 10(13), rare enough, to be sure, but nevertheless in a range that is comfortably accessible by experiment. It is the purpose of this Account to describe the recent advances in **combinatorial** biochemistry that have made it possible for us to explore the abundance and diversity of **catalysts** existing in nucleic acid sequence space.

L22 ANSWER 52 OF 56 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:234472 HCAPLUS
DOCUMENT NUMBER: 124:282894
TITLE: Directed **evolution** of subtilisin E in Bacillus subtilis to enhance total activity in aqueous dimethylformamide
AUTHOR(S): You, L.; Arnold, F. H.
CORPORATE SOURCE: Div. Chem. and Chem. Engineering, California Institute Technology, Pasadena, CA, 91125, USA
SOURCE: Protein Engineering (1996), 9(1), 77-83
CODEN: PRENE9; ISSN: 0269-2139
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Sequential rounds of error-prone PCR to introduce **random** **mutations** and screening of the resultant mutant libraries have been used to enhance the total **catalytic** activity of subtilisin E significantly in a non-natural environment, aq. DMF. Seven DNA substitutions coding for three new amino acid substitutions were identified in a mutant isolated after two addnl. **generations** of directed **evolution** carried out on 10M subtilisin E, previously 'evolved' to increase its specific activity in DMF. A Bacillus subtilis-Escherichia coli shuttle vector was developed in order to increase the size of the mutant library that could be established in B. subtilis, and the stringency of the screening process was increased to reflect total as well as specific activity. This directed **evolution** approach has been extremely effective for improving enzyme activity in a non-natural environment; the resulting evolved 13M subtilisin exhibits specific **catalytic** efficiency towards the hydrolysis of a peptide substrate, succinyl-Ala-Ala-Pro-Phe-p-nitroanilide, in a 60% DMF soln. that is three times that of the parent 10M and 471 times that of wild type subtilisin E. The total activity of the 13M culture supernatant is enhanced 16-fold over that of the parent 10M.

L22 ANSWER 53 OF 56 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN

Search completed by David Schreiber 308-4292

Zhou 09/909,038

ACCESSION NUMBER: 95:664275 SCISEARCH
THE GENUINE ARTICLE: RX194
TITLE: FROM MOLECULAR DIVERSITY TO **CATALYSIS** - LESSONS FROM THE IMMUNE-SYSTEM
AUTHOR: SCHULTZ P G (Reprint); LERNER R A
CORPORATE SOURCE: UNIV CALIF BERKELEY, HOWARD HUGHES MED INST, DEPT CHEM, BERKELEY, CA, 94720 (Reprint)
COUNTRY OF AUTHOR: USA
SOURCE: SCIENCE, (29 SEP 1995) Vol. 269, No. 5232, pp. 1835-1842. ISSN: 0036-8075.
DOCUMENT TYPE: General Review; Journal
FILE SEGMENT: PHYS; LIFE; AGRI
LANGUAGE: ENGLISH
REFERENCE COUNT: 117

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB By combining the enormous molecular diversity of the immune system with basic mechanistic principles of chemistry, one can produce **catalytic** antibodies that allow control of reactions in ways heretofore not possible. Mechanistic and structural studies of these antibodies are also providing insights into important aspects of enzymatic **catalysis** and the **evolution** of **catalytic** function, Moreover, the ability to rationally direct the immune response to generate selective **catalysts** for reactions ranging from pericyclic and redox reactions to cationic rearrangement reactions underscores the chemical potential of this and other large **combinatorial** libraries.

L22 ANSWER 54 OF 56 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1994:312373 HCAPLUS
DOCUMENT NUMBER: 120:312373
TITLE: Studies of mordenite by Monte Carlo method. I. Si, and Al distribution in framework of parent mordenite
AUTHOR(S): Sun, Pingchuan; Li, Baohui; Jin, Qinghua; Wang, Jingzhong; Ding, Datong; Wang, Qunhai; Sun, Yongkang
CORPORATE SOURCE: Nankai Univ., Peop. Rep. China
SOURCE: Huaxue Wuli Xuebao (1993), 6(6), 534-41
CODEN: HWXUE4; ISSN: 1003-7713
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB The distribution of Al atoms in the framework of parent mordenites was simulated by two models. According to the first one, Model-I, the distribution of Al atoms was constrained only by Loewenstein's rule. In Monte Carlo simulation, the sampling configurations were created by using a **random** no. **generator** which positions Al atoms in a representative portion of the framework (27 unit cells) randomly and does not allow the presence of any couple of nearest-neighboring Al-Al. For each sampling configuration, the nos. of five types of building units {Si(n-Al); n = 0-4} were counted up by computerization. The populations of the building units for given Si/Al ratio were obtained by taking an av. from a sample space of a large enough size. Distribution Model-II superimposes on Model-I a second, weaker constraint which minimized the no. of Al-Al next-nearest neighbors in its sampling configurations. The calcd. populations of the building units {Si(n-Al)} could be compared with the relative intensities of the 29Si MAS NMR spectrum of the parent mordenite sample with corresponding Si/Al framework ratio. The Monte Carlo simulation based on distribution Model-II gave much better results than the Model-I coinciding with 29Si MAS NMR observations. The results indicate that the distributions of Al atoms in the framework of parent mordenites are subject to the constraint of Loewenstein's rule, which

forbids the presence of Al-Al nearest-neighbors; superimposed on this is a second weaker constraint that the Al-Al are avoided to be next-nearest neighbor. Based on the distribution Model-II, the relative populations of type Al(m-Al) (m = 0-3) were calcd. as well. Because both calcd. {Si(n-Al)} and {Al(m-Al)} were obtained from the same Monte Carlo sample space, their correlation was then established on reasonable theor. foundation. The former, {Si(n-Al)}, can be checked by 29Si MAS NMR observation exptl., the latter, {Al(m-Al)}, is connected with the **catalytic** properties of the parent mordenites.

L22 ANSWER 55 OF 56 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 92262458 MEDLINE
DOCUMENT NUMBER: 92262458 PubMed ID: 1584777
TITLE: Semisynthetic **combinatorial** antibody libraries: a chemical solution to the diversity problem.
AUTHOR: Barbas C F 3rd; Bain J D; Hoekstra D M; Lerner R A
CORPORATE SOURCE: Department of Molecular Biology, Scripps Research Institute, La Jolla, CA 92037.
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1992 May 15) 89 (10) 4457-61. Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199206
ENTRY DATE: Entered STN: 19920626
Last Updated on STN: 19920626
Entered Medline: 19920616

AB The properties of naivete and large diversity are considered to be essential starting features for **combinatorial** antibody libraries that eschew immunization by **evolution** in vitro. We have prepared large libraries with such properties by using **random** oligonucleotide synthesis, which has the potential to create approximately 10(20) complementarity-determining regions for antibody heavy chains. When **combined** with light chains and expressed on phage surfaces, high-affinity antibodies could be selected from 5.0 x 10(7) Escherichia coli transformants. Remarkably, antibodies selected only for binding displayed both general **structural** features known to be important in nature's own antibodies and specific consensus sequences thought to be critical for interaction with the hapten against which the library was selected. Semisynthetic and ultimately totally synthetic **combinatorial** libraries when coupled with **mutation** and selection procedures should replace immunization for **generation** of reagent, therapeutic, and **catalytic** antibodies.

L22 ANSWER 56 OF 56 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1980:53851 HCAPLUS
DOCUMENT NUMBER: 92:53851
TITLE: Terminal transferase - a "**random generator**"?
AUTHOR(S): Reitz, Manfred
CORPORATE SOURCE: Inst. Physiol. Chem., Johannes Gutenberg-Univ., Mainz, 6500, Fed. Rep. Ger.
SOURCE: Umschau in Wissenschaft und Technik (1979), 79(23), 749-50
CODEN: UWTCAZ; ISSN: 0041-6347
DOCUMENT TYPE: Journal; General Review
LANGUAGE: German

Search completed by David Schreiber 308-4292

Zhou 09/909,038

AB A review with 4 refs. of the properties of possible biol. function of terminal nucleotidyltransferase, an enzyme that **catalyzes** the addn. of deoxyribonucleotides to DNA primers without a requirement for a template and which can thus generate new genetic information at random. The possible role of this enzyme in maturation of immunocompetent lymphocytes is discussed.

Search completed by David Schreiber 308-4292

Zhou 09/909,038

=> d his 1

(FILE 'MEDLINE, HCAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 13:36:27 ON 24 SEP 2003)
L7 8 DUP REM L6 (3 DUPLICATES REMOVED)

=> d que l7
L1 6564 SEA WOLF D?/AU
L2 35 SEA GERLACH O?/AU
L3 499 SEA BAERNS M?/AU
L4 7040 SEA (L1 OR L2 OR L3)
L5 19 SEA L4 AND CATALY? AND EVOLUTION?
L6 11 SEA L5 AND COMBINATORIAL?
L7 8 DUP REM L6 (3 DUPLICATES REMOVED)

=> d ibib abs l7 1-8

L7 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2001:499179 HCAPLUS
DOCUMENT NUMBER: 135:304157
TITLE: Fundamental and **combinatorial** approaches in the search for and optimization of **catalytic** materials for the oxidative dehydrogenation of propane to propene
AUTHOR(S): Buyevskaya, O. V.; Bruckner, A.; Kondratenko, E. V.; **Wolf, D.; Baerns, M.**
CORPORATE SOURCE: Institute for Applied Chemistry, Berlin, D-12489, Germany
SOURCE: Catalysis Today (2001), 67(4), 369-378
CODEN: CATTEA; ISSN: 0920-5861
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An **evolutionary** approach was applied to create five generations of .alpha.-Al2O3-supported multi-metal-oxides to be used as **catalytic** materials for the oxidative dehydrogenation of propane at 773 K. Each generation consisted of 56 differently composed materials, i.e., a total amt. of 280 materials. These **catalytic** materials were tested in parallel. For the best materials propene yields from 7% (1st generation) to 9% (5th generation) were achieved. Some of these superior **catalysts** were characterized by XRD, XPS and EPR. A correlation between **catalytic** performance and the Mg/V ratio on the surface was found. Based on the structural knowledge obtained, from which the requirement of isolated or at least weakly interacting vanadium sites was derived, VOx (2.8 wt.%)/MCM-48 and VOx (2.8 wt.%)/MCM-41 **catalysts** with a high dispersion of vanadia were used as ref. giving a maximal propene yield of 17 and 15%, resp.
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 8 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 2001:615216 SCISEARCH
THE GENUINE ARTICLE: 456JG
TITLE: Characterisation of vanadium-oxide-based **catalysts** for the oxidative dehydrogenation of propane to propene
AUTHOR: Kondratenko E V (Reprint); Buyevskaya O V; **Baerns M**
CORPORATE SOURCE: Berlin Adlershof ACA, Inst Appl Chem, Richard Willstatter

Search completed by David Schreiber 308-4292

Str 12, D-12489 Berlin, Germany (Reprint); Berlin Adlershof ACA, Inst Appl Chem, D-12489 Berlin, Germany
COUNTRY OF AUTHOR: Germany
SOURCE: TOPICS IN CATALYSIS, (15 JUN 2001) Vol. 15, No. 2-4, pp. 175-180.
Publisher: KLUWER ACADEMIC/PLENUM PUBL, 233 SPRING ST, NEW YORK, NY 10013 USA.
ISSN: 1022-5528.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 20

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The study is based on the previous development of alpha -Al2O3-supported multi-metal-oxide materials for oxidative dehydrogenation of propane by applying a **combinatorial** approach (773 K, ambient pressure, a feed composition of C3H8; O-2: N-2 =30:10:60 and 40:20:40). For further improvement of **catalytic** materials, fundamental insights were derived from oxygen transient experiments and XRD as well as XPS studies. Fitting transient experiments showed that irreversible and dissociative adsorption on two active centers provides a good description of the transient oxygen responses over all the **catalytic** materials studied. The composition of these materials influenced strongly the apparent first-order rate constant of oxygen activation. Based on the characterisation data it was found that an optimal bulk concentration (2.6-8.3 wt%) of VOx species on the support and their distribution on the surface are an essential requirement for the selective oxidative dehydrogenation of propane to propene.

L7 ANSWER 3 OF 8 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 2001:295923 SCISEARCH
THE GENUINE ARTICLE: 417RK
TITLE: High-throughput synthesis and screening of **catalytic** materials - Case study on the search for a low-temperature **catalyst** for the oxidation of low-concentration propane
AUTHOR: Rodemerck U; **Wolf D**; Buyevskaya O V; Claus P; Senkan S; **Baerns M (Reprint)**
CORPORATE SOURCE: Inst Appl Chem, Berlin Adlershof Richard Willstatter Str 12, D-12489 Berlin, Germany (Reprint); Inst Appl Chem, D-12489 Berlin, Germany; Univ Calif Los Angeles, Dept Chem Engn, Los Angeles, CA 90095 USA
COUNTRY OF AUTHOR: Germany; USA
SOURCE: CHEMICAL ENGINEERING JOURNAL, (15 MAR 2001) Vol. 82, No. 1-3, Sp. iss. SI, pp. 3-11.
Publisher: ELSEVIER SCIENCE SA, PO BOX 564, 1001 LAUSANNE, SWITZERLAND.
ISSN: 1385-8947.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 19

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Low-temperature **catalysts** for the total combustion of low-concentration propane in air have been searched for applying a **combinatorial** approach including an optimization procedure based on a genetic algorithm. A ist generation of **catalysts** was prepared by impregnation of TiO2 and Fe2O3 materials with randomly mixed solutions of eight individual compounds (H-2[PtCl6]. xH(2)O, (NH4)(2)PdCl6, RhCl3. 2H(2)O, RuCl3.H2O, H[AuCl4]. 3H(2)O, Ag lactate, Cu(NO3)(2), Mn(NO3)(2)) considered as potential **catalytic**

compounds. After parallel testing of the Ist generation of the **catalytic** materials applying high-throughput testing equipment the most active **catalysts** were chosen to create a 2nd and after its testing a 3rd generation, respectively. A genetic algorithm was applied to set the compositions of the **catalytic** compounds of the 2nd and 3rd generation. Fe2O3 was not used as support for the succeeding generations since it lead to significantly inferior **catalytic** performances than TiO2. The optimization strategy led to improved **catalysts**. Most of the final material converted propane to CO2 at 150 degreesC, the best ones oxidized propane even at 50 degreesC.

Furthermore, the goal was pursued to compare the performance of two different high-throughput testing equipments. In both cases the ranking of 45 **catalysts** was nearly the same. (C) 2001 Elsevier Science B.V. All rights reserved.

L7 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:190991 HCAPLUS
DOCUMENT NUMBER: 132:228064
TITLE: Method for producing active and/or selective solid **catalysts** from inorganic or organometallic materials
INVENTOR(S): **Wolf, Dorit**; Buyevskaya, Olga; **Baerns, Manfred**; Rodemerck, Uwe; Claus, Peter
PATENT ASSIGNEE(S): Institut Fur Angewandte Chemie Berlin-Adlershof E.V., Germany
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000015341	A2	20000323	WO 1999-DE2956	19990910
WO 2000015341	A3	20010215		
W: JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19843242	A1	20000323	DE 1998-19843242	19980911
EP 1124636	A2	20010822	EP 1999-969046	19990910
EP 1124636	B1	20021218		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002524251	T2	20020806	JP 2000-569920	19990910
AT 229844	E	20030115	AT 1999-969046	19990910
PRIORITY APPLN. INFO.:			DE 1998-19843242 A	19980911
			WO 1999-DE2956 W	19990910

AB The invention relates to an **evolutionary** method for producing **catalysts**. In a first step (i), components are selected and added to a library of substances. Mixts. of these individual materials are then produced randomly by random selection. In the second step (ii), this first generation of **catalysts** produced is **catalytically** tested. **Catalyst**-optimized materials from step (ii) are phys./chem. characterized for reproducible prodn. in step (iii) and form the basis for a second generation of **catalysts**. This second generation is produced gradually from the successful materials of the first generation using biol. **evolutionary** methods such as crossing and mutation, and subjected to steps (ii) and (iii). For the

second and subsequent iterations, the most successful **catalysts** of all the generations are taken as a basis in each case, the total no. of said **catalysts** being 1 to 50% of the **catalysts** of a generation. The iterations are continued until no further improvement is obsd. in the **catalytic** properties of the materials in terms of activity/selectivity, for the reaction concerned.

L7 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2000:891929 HCAPLUS
DOCUMENT NUMBER: 134:71932
TITLE: Ethylene and propene by oxidative dehydrogenation of ethane and propane. 'Performance of rare-earth oxide-based **catalysts** and development of redox-type **catalytic** materials by **combinatorial** methods'
AUTHOR(S): Buyevskaya, O. V.; **Wolf, D.; Baerns, M.**
CORPORATE SOURCE: Institute for Applied Chemistry, Berlin-Aldershof, Berlin, D-12489, Germany
SOURCE: Catalysis Today (2000), 62(1), 91-99
CODEN: CATTEA; ISSN: 0920-5861
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Selected aspects related to the mode of reactor operation and to the development of **catalysts** for the oxidative dehydrogenation of ethane and propane to their resp. olefins are dealt with. The differences in the **catalytic** conversion when applying ethane or propane on rare-earth-oxide (REO)-based **catalysts** leading to the ignition of the reaction mixt. are discussed. For ethane dehydrogenation, ethylene yields up to 46% were achieved by non-isothermal operation. Non-isothermicity was caused by ignition of the reaction and the resultant heat prodn. The formation of ethylene occurred via thermal pyrolysis and oxidative dehydrogenation. In general, autothermal operation looks promising for the prodn. of ethylene from ethane. The advantage of REO-based **catalysts** as compared to noble metals like Pt is their high thermal stability. There are, however, limitations regarding to dehydrogenation of propane to propene in the autothermal mode. A high propene yield is not possible when applying such conditions since C-C scission results in a decrease of propene selectivity. The search for new active and selective formulations operating at low temps. is, therefore, still timely. Against this requirement, special attention was given to a **combinatorial** and **evolutionary** approach for the selection and optimization of **catalytic** materials for the oxidative dehydrogenation of propane; selected exptl. results as a proof of principle are presented.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2000:564776 HCAPLUS
DOCUMENT NUMBER: 133:355774
TITLE: An **evolutionary** approach in the **combinatorial** selection and optimization of **catalytic** materials
AUTHOR(S): **Wolf, D.**; Buyevskaya, O. V.; **Baerns, M.**
CORPORATE SOURCE: Institut fur Angewandte Chemie Berlin-Adlershof e. V., Berlin, D-12484, Germany

Zhou 09/909,038

SOURCE: Applied Catalysis, A: General (2000), 200(1-2), 63-77
CODEN: ACAGE4; ISSN: 0926-860X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A methodical basis of the **evolutionary** method for selection and optimization of heterogeneous **catalytic** materials was developed. For validation, the oxidative dehydrogenation of propane was used as a model reaction. Various oxides (V2O5, MoO3, MnO2, Fe2O3, GaO, MgO, B2O3, La2O3) were chosen as primary components for the generation of **catalytic** materials. The first generation consisting of 56 **catalytic** materials was created by combination of the primary components in a stochastic manner. The materials of each preceding generation were selected based on the **catalytic** results obtained and subjected to an **evolutionary** procedure applying mutation and crossover operators to create further generations of **catalytic** materials of different qual. and quant. compns. For illustration, four generations were created with a total no. of tested **catalytic** materials of 224. As a result of the preliminary optimization procedure an increase in the propene yield was achieved with increasing no. of generations; the results can be certainly improved by screening further generations of **catalytic** materials. Under std. conditions used for testing (T=500.degree.C, C3H8/O2=3, p(C3H8)=30 Pa), the highest C3H6 yield amounted to 9.0% (S=57.4%) in the 3rd generation on V0.22Mg0.47Mo0.11Ga0.20Ox.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:91294 HCAPLUS
TITLE: A **combinatorial** and **evolutionary** approach to the selection and testing of **catalytic** materials for selective hydrocarbon oxidation
AUTHOR(S): **Baerns, Manfred**; Buyevskaya, Olga; **Wolf, Dorit**
CORPORATE SOURCE: Institute for Applied Chemistry Berlin-Adlershof, Berlin, D-12484, Germany
SOURCE: Book of Abstracts, 217th ACS National Meeting, Anaheim, Calif., March 21-25 (1999), CATL-050. American Chemical Society: Washington, D. C.
CODEN: 67GHA6
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English

AB Various **catalytic** compds. being considered essential for selective hydrocarbon oxidn. were selected. These compds. were mixed in a stochastic manner resulting in the first generation of **catalysts**. A certain amt. of **catalysts** derived from the first generation as the best ones with respect to selectivity and yield resp. were subjected to an **evolutionary** method for prepg. further generations of **catalyts**; this **evolutionary** method included mutation, cross-over and random mixing. It was shown that this method included mutation, cross-over and random mixing. It was shown that this method leads to an improved performance of the final **catalyst** compn. obtained compared to up-to-then results on selectivity and yield.

L7 ANSWER 8 OF 8 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 1999:228745 SCISEARCH
THE GENUINE ARTICLE: 176JP

Search completed by David Schreiber 308-4292

Zhou 09/909,038

TITLE:	A **combinatorial** and **evolutionary** approach to the selection and testing of **catalytic** materials for selective hydrocarbon oxidation
AUTHOR:	**Baerns M (Reprint)**; Buyevskaya O; **Wolf D**
CORPORATE SOURCE:	INST APPL CHEM BERLIN ADLERSHOF, D-12484 BERLIN, GERMANY
COUNTRY OF AUTHOR:	GERMANY
SOURCE:	ABSTRACTS OF PAPERS OF THE AMERICAN CHEMICAL SOCIETY, (21 MAR 1999) Vol. 217, Part 2, pp. 50-CATL. Publisher: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036. ISSN: 0065-7727.
DOCUMENT TYPE:	Conference; Journal
LANGUAGE:	English
REFERENCE COUNT:	0

Search completed by David Schreiber 308-4292